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TETANUS:

Analysis of One Thousand Cases.

(PRESIDENTIAL ADDRESS.)

BY

SIR DAVID BRUCE, C.B., F.R.S., F.R.C.P.

Surgeon-General, Army Medical Service.

Chairman of the War Office Committee for the Study of Tetanus.

(Paper read at a Meeting of the Society of Tropical Medicine and Hygiene, Friday, October 19th, 1917).

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Presidential Address.

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I. INTRODUCTION.

I must apologise to the Society for bringing before it, in a presidential address, the subject of tetanus, which can hardly be strictly called a tropical disease, although it is true that it is of more common occurrence in the tropics than in temperate climates. My excuse is that this is a time of war, and tetanus has an important place among war diseases. Moreover, part of my work, since the beginning of the war, has been to supervise the investigation and treatment of tetanus occurring in our home military hospitals. I therefore thought it would be better to address you on a subject of practical importance at the present time. Interest in tick fever, sleeping sickness, and other purely tropical diseases has lapsed for the time being. They seem, in truth, to belong to a past existence.

In this paper it must be understood that only cases of tetanus arising in England are dealt with. Many cases have occurred in France among the wounded before their transfer to home hospitals. These have been analysed, at least in part, by Sir WILLIAM LEISHMAN and Major SMALLMAN. An attempt to amalmagate these cases with the cases occurring in England was made, but was found to be impracticable on account of the want of sufficient data.

In regard to the origin of this work on tetanus the history may be given briefly. In October, 1914, after returning from Nyasaland, I received orders to report at the War Office on the 1st November, 1914. In his

letter of instruction, Sir ALFRED KEOGH, the Director-General, wrote:—"It is hoped that you will direct your attention specially to the subject of tetanus, with a view to elucidating the problems of causation and cure. To this end military hospitals will be instructed to notify cases to you, and send you such particulars as you may require."

The taking up of this work was, therefore, due to a request from the Director-General. The cases which have been notified up to the present time number a thousand, and form the subject of this paper.

To Lady BRUCE fell the work of entering under the various headings the different items of information contained in the Report Forms. This has been a very arduous piece of work, and it is no exaggeration to say that it has taken an average of some five hours a day during the last three years to accomplish.

As Lady BRUCE is purely a voluntary worker, I am sure you will agree that our heartiest thanks are due to her for the enormous amount of trouble she has taken in this matter. In March, 1916, a Tetanus Committee was formed at the suggestion of Professors WALLER and PLIMMER and Captain GOLLA, and the first meeting took place on the 7th March of that year. A Memorandum on Tetanus,* which is now in its third edition, was prepared by the Committee and circulated, the Tetanus Report Forms were revised, and a new Form for Inspectors of Tetanus circulated. At the present there are some forty inspectors in different parts of the country supervising the study and treatment of this disease. It is not possible to mention all these officers by name, but they also deserve our best thanks for the excellent work they have done. I have already published several analyses of cases of tetanus treated in home hospitals, and this paper is merely a bringing together of the previous work, making the figures dealt with up to 1,000.

Members of the Committee have written several papers to the medical journals with a view to giving medical officers the latest developments in our knowledge of tetanus. A list of these papers is given in an appendix. The Committee has also instituted original investigations, some of which are bearing fruit. Miss ROBERTSON and Captain TULLOCH, R.A.M.C., have been working at the anaerobic fauna of septic wounds, and especially the tetanus bacillus. These researches have been carried out at the Lister Institute.

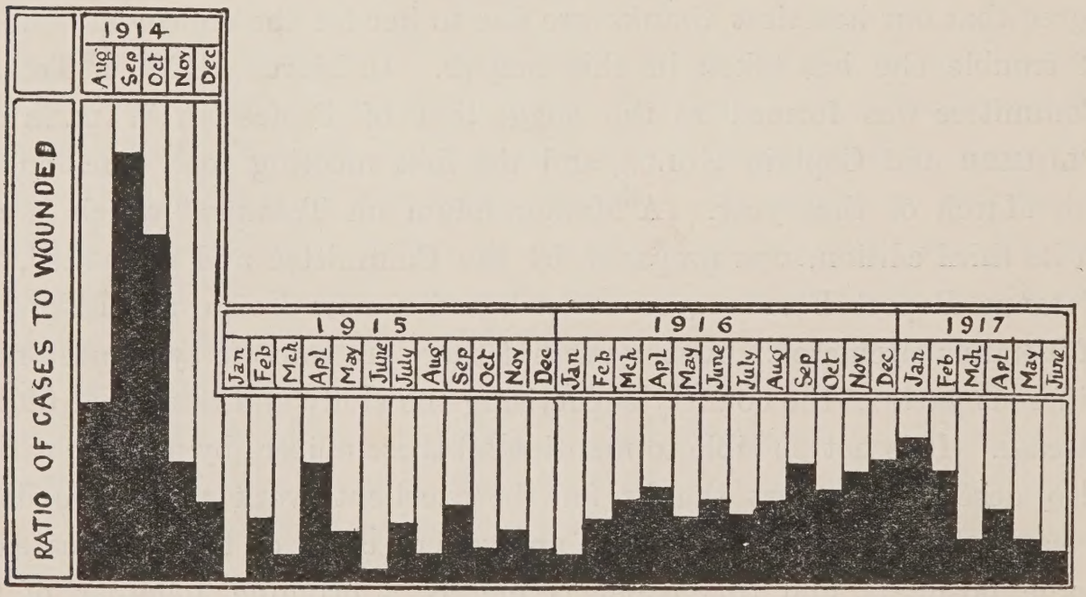
* Copies of these forms are printed in the appendix.

Professor SHERRINGTON has also been studying the effect of the tetanus toxin and antitoxin on monkeys at Oxford. The expenses of these various researches are being borne by the Lister Institute.

II. THE RATIO OF THE NUMBER OF CASES OF TETANUS TO THE NUMBER OF WOUNDED.

In regard to the incidence of tetanus among the wounded treated in home hospitals it is impossible at present to deal fully. The number of wounded from overseas is not yet available for publication. I am, however, enabled to give some information in the form of a diagram, for which I am indebted to Colonel WEBB, R.A.M.C., and Captain HARWOOD, of the Statistical Department of the Army Medical Staff.

DIAGRAM I.



RATIO OF CASES OF TETANUS TO WOUNDED.

From the above diagram it will be seen that the ratio of the number of cases of tetanus to the number of wounded is about six times as high in September, 1914, as it is in November, and nine times as high as in December of the same year.

It will also be seen that the ratio remains at the lower level until June, 1917. There is, however a tendency to rise in 1916, so that the ratio between September, 1914, and December, 1916, is only $4\frac{1}{2}$ times as great. This upgrade movement is probably due to an improve-

ment in the diagnosis of mild cases of local tetanus, which at the beginning of the war were possibly overlooked. This would naturally raise the ratio of the incidence. In regard to the sudden drop in the ratio in December, 1914, I shall return to this later.

It may be asked what proportion of wounded men are attacked by tetanus in home hospitals. This cannot be answered with any attempt at accuracy at present, but judging from data sent in from various districts it may be put down at one per thousand. It is a thousand to one against a wounded man in England contracting tetanus. This, however, is not the true incidence of tetanus among the wounded of this war. The wounded in France and the wounded in England are not separate and distinct populations. The wounded in England were at one time the wounded in France. Many cases of tetanus, probably about 800, have occurred overseas. These added to the English cases would give the true incidence if every wounded man came over from France. But, again, many of the wounded are treated in France, and return to duty without coming over to England. It is, therefore, not possible at present to give the true incidence for this war, although roughly it may be put down at about two per thousand.

III. THE DISTRIBUTION OF CASES OF TETANUS FROM AUGUST, 1914, TO JUNE, 1917.

Diagram II.

CASES OF TETANUS BY MONTHS FROM DATE OF WOUND.

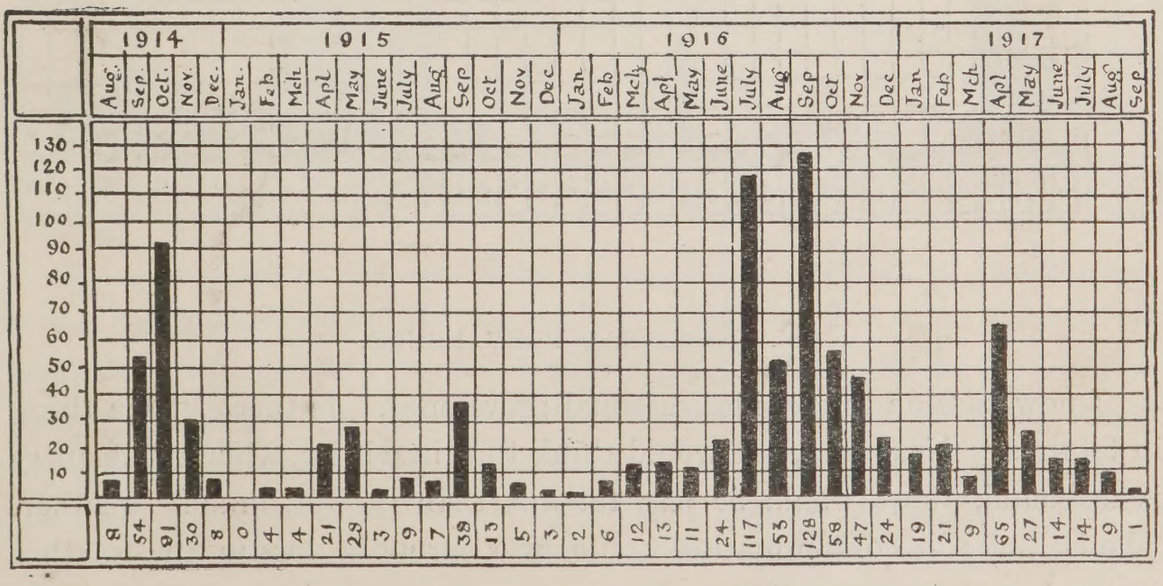
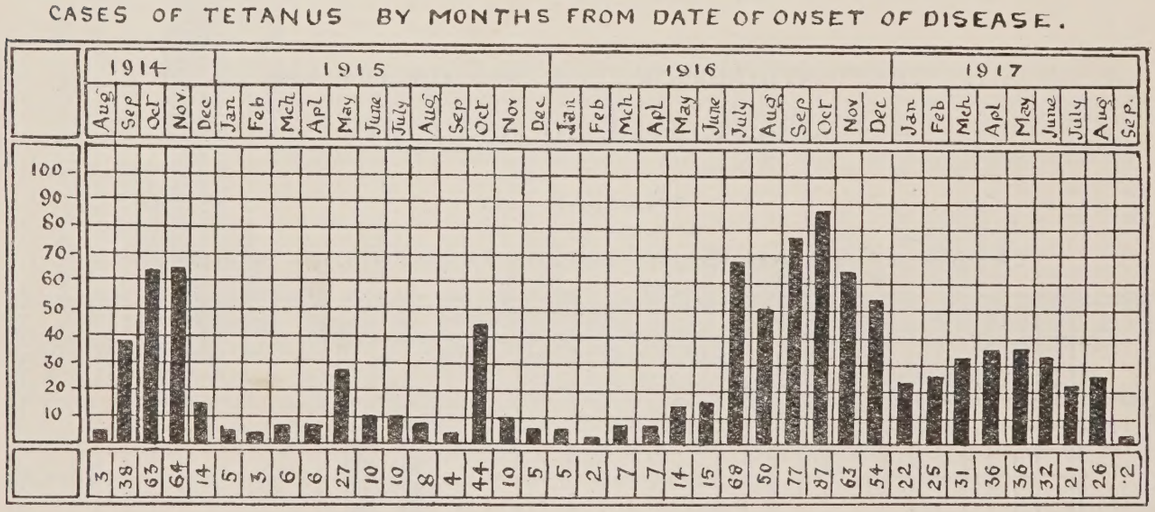

1914
1915
1916
1917
Aug. Sep. Oct. Nov. Dec. Jan. Feb. Mch. Apl. May June July Aug. Sep Oct Nov Dec Jan. Feb Mch Apl May June July Aug. Sep Oct Nov Dec Jan. Feb Mch. Apl May June July Aug. Sep
130
120
110
100
90
80
70
60
50
40
30
20
10
8 54 91 30 8 0 4 4 21 29 3 9 7 38 13 5 3 2 6 12 13 11 24 117 53 128 58 47 24 19 21 9 65 27 14 14 9 1

Diagram II. merely represents the number of cases of tetanus which have been treated in home military hospitals since the beginning of the war. They are taken from the date of the wound, not from the date of onset of the disease. For example, in August, 1914, there were eight men wounded, who, sooner or later, developed tetanus. The figures have no relation to the number of wounded or the number of troops engaged. It shews periods of activity and inactivity in the fighting line. For example, the eight men in August, 1914, were wounded at the battle of Mons, the 54 in September at the battle of the Marne. The cases in October and November were due to wounds received probably at La Bassée and Ypres. The rise in September, 1915, marks the battle of Loos; in July, 1916, the battle of the Somme, and so on.

Diagram III. represents the number of cases of tetanus which have been treated in home military hospitals since the beginning of the war. They are taken from the date of the onset of the disease. For example, in August, 1914, there were three wounded men in England who had been attacked by tetanus.

DIAGRAM III.


CASES OF TETANUS BY MONTHS FROM DATE OF ONSET OF DISEASE.
1914
1915
1916
1917
Aug. Sep Oct Nov Dec Jan Feb Mch Apl May June July Aug. Sep Oct Nov Dec Jan Feb Mch Apl May June July Aug. Sep Oct Nov Dec Jan Feb Mch Apl May June July Aug. Sep.
100
90
80
70
60
50
40
30
20
10
3 38 63 64 14 5 3 6 6 27 10 10 8 4 44 10 5 5 2 7 7 14 15 68 50 77 87 63 54 22 25 31 36 36 32 21 26 12

IV. SEASONAL PREVALENCE.

I now pass on to consider seasonal prevalence. Is there such a thing in tetanus? Naturally, one would think that in winter, when the country is icebound, there would be less tetanus than in wet, muddy weather. The risk of soil contamination would also surely be less in fine weather

when the ground is hard. Can this be demonstrated by means of these figures?

Diagram I. gives the ratio of cases of tetanus to wounded, and if such a thing as marked seasonal prevalence prevailed, it might be seen here. But no such evidence emerges.

V. CLASSIFICATION OF THE VARIOUS TYPES OF TETANUS.

In the latest "tetanus report form" the disease is classified under four heads:—

(a) Trismus, the earliest symptom.

1. Tetanus with complete closure of jaws (teeth cannot be separated), developing within 24 hours from onset of symptoms.
2. Tetanus with complete closure of jaws, developing after more than 24 hours.
3. With incomplete closure of jaws. Mouth can be partially opened.

(b) Trismus occurring after other symptoms of tetanus have shewn themselves.

(c) General tetanus, without trismus.

(d) Local tetanus, without trismus.

As the classification has only been in use for a short time, it is not possibly to classify in this way the 1,000 cases under consideration. It is only possible to classify them under the headings of (1) General *(a)* with trismus; *(b)* without trismus; and (2) Local without trismus.

It is by no means easy in many cases to decide whether a case is one of generalised or localised tetanus. By generalised tetanus is meant the occurrence of spasticity or rigidity in muscles distant from the site of wound. Trismus is the most common initial symptom in generalised tetanus.

In local tetanus the spasticity or rigidity is confined to the muscles in the neighbourhood of the wound. In a case of this kind arising, for example, from a wound in the right leg, the toxin may be pictured as passing up the nerves and affecting the motor cells of the cord which regulate the nervous supply to the muscles of the wounded leg. In these cases the toxin does not appear to proceed farther up the cord or to be capable of spreading by the blood stream. Hence the symptoms of

twitching, spasm, or rigidity, are confined to the wounded limb. Local tetanus may be looked upon as a much modified variety of the original disease, or even as a new type, due to the action of the prophylactic injection of antitoxin.

In general tetanus, on the other hand, the toxin molecules may be pictured as gaining entrance to the circulation, and so reaching all parts of the body. In this case trismus is frequently the first symptom, either on account of some selective quality towards the toxin inherent in the fifth nerve, or on account of the shortness of the nervous route between the masseter muscles and the central nervous system. The toxin has a shorter distance to pass up the nerve from the nerve-ending to the nerve-cell.

On examining the thousand cases under consideration, it was found that 896 could be placed in the general, and 99 in the local group; in five it was doubtful to which group they belonged. The symptom of trismus is recorded in 607 cases. In 289 cases of general tetanus there is no record of trismus having been a symptom.

This is represented in the following table:—

TABLE I.

No. of Cases.	Type of Tetanus.	Percentages.
607	General with Trismus	60·7
289	General without Trismus	28·7
99	Local without Trismus	10·0
5	Doubtful	0·5

Table II. represents the proportion of general to local tetanus as reported at different periods of the war.

TABLE II.

Type.	Percentages in the Six Analyses.					
	1	2	3	4	5	6
General	97·5	98·0	89·0	61·0	81·0	80·0
Local	0·8	2·0	11·0	28·0	19·0	20·0

It will be seen that the proportion of cases of local tetanus becomes larger in each succeeding analysis, due no doubt in great part to the introduction of the prophylactic injection of antitoxin, and also to the greater number of local cases being diagnosed as tetanus.

VI. THE PERIOD OF INCUBATION.

(a) At daily intervals.

The incubation period, or the number of days which elapse between the date of wound and the onset of tetanus symptoms, is represented by the following curve:—

CURVE A.

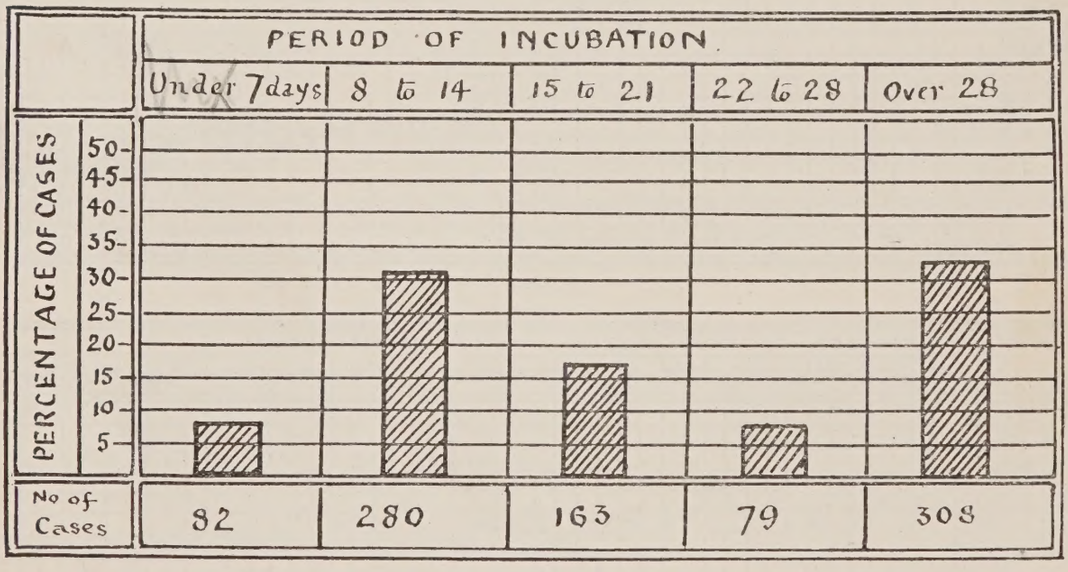
NUMBER OF DAYS AFTER WOUND
NUMBER OF CASES
NUMBER OF DAYS AFTER WOUND (CONTINUED)
No OF CASES
UMBER OF DAYS AFTER WOUND (CONTINUED)
No OF CASES

Curve A shews the number of cases which occurred on each day after the date of the wound. The shortest period of incubation was two days, the longest a year. One case put down at 786 days is a very doubtful one, and may be ignored. The greatest number of cases occurred on the ninth day.

(b) At weekly intervals.

Diagram IV. gives the percentage of cases of tetanus occurring at weekly intervals. From it it will be seen that in the thousand cases under consideration, 8·8 per cent. of the wounded are attacked during the first week, 30·7 per cent. during the second, and as many as 33·6 per cent. after four weeks. This diagram is very different from what obtained in pre-serum days, and as we shall afterwards see, is due to the prophylactic injection of antitoxin given soon after the wound is received.

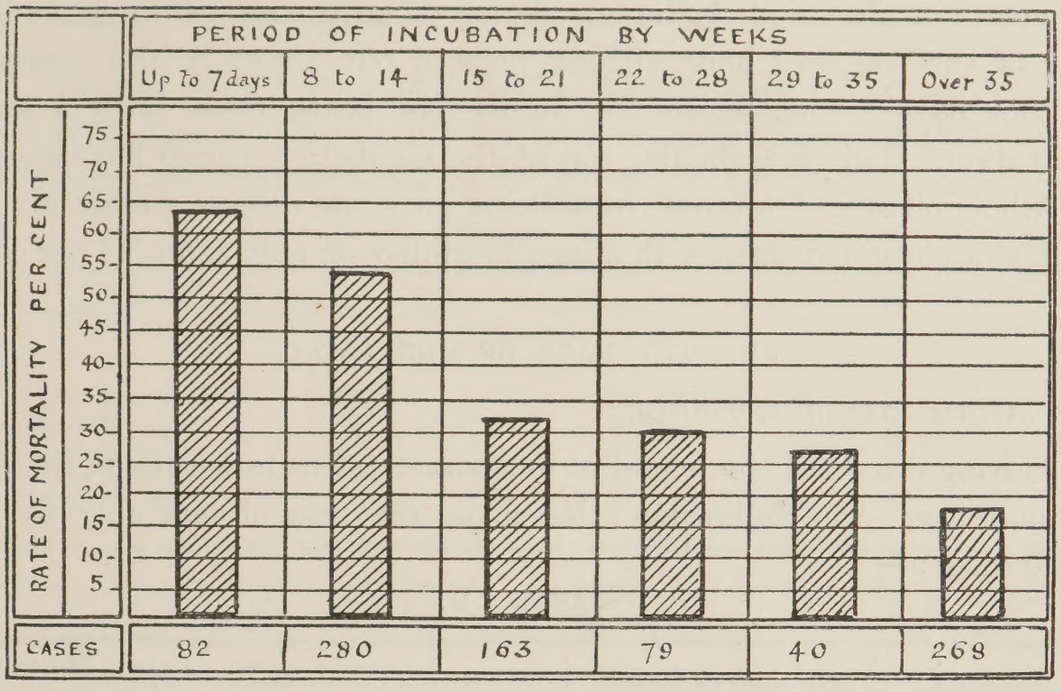
DIAGRAM IV.



(c) Length of incubation in relation to the rate of mortality.

Diagram V. gives the length of incubation in relation to the rate of mortality. In 82 cases, with an incubation of seven days or under, the rate of mortality was 63·4 per cent.; in 268 cases with an incubation of more than 35 days, the mortality has fallen to 16·8. From this diagram it is abundantly plain that the shorter the period of incubation the higher the rate of mortality.

DIAGRAM V.



(d) The variation in the period of incubation since the beginning of the war.

This lengthening out of the period of incubation has taken place during the war. Few prophylactic injections of antitoxin were given during the first year, since by far the greater number of the cases in that year occurred during the first months, before the administration of prophylactic injections had got under weigh.

The following table gives the number, in percentages, of cases of tetanus with short, medium and long incubation periods which have occurred since the beginning of the war. From it will be seen that in the first year there were 47 per cent. of cases with a short incubation, whereas in the last analysis this has fallen to 10 per cent. In 1914-15, there were only 6·4 per cent. of cases with a long incubation period; but this rose at the beginning of 1917 to 69 per cent.

TABLE III.—INCUBATION PERIODS.

Analyses.	Up to 10 days per cent.	11 to 22 days per cent.	More than 22 days per cent.
1914–15.	47·0	46·4	6·4
1915–16.	15 5	48·8	35·6
Aug. to Oct., 1916.	14·0	43·8	42·1
Oct. to Dec., 1916.	12·6	26·3	61·1
Dec. 1916, to Mar., 1917.	10·0	21·0	69·0

I think this is a remarkable result, and can be taken as a measure of the action of the prophylactic inoculation of antitoxin. During the first year of the war, as I have already pointed out, many of the wounded did not receive this, hence the number of acute cases with a short incubation. This lengthening out of the incubation period has changed the whole picture of tetanus, from being an acute disease almost always fatal, to a chronic disease with a case mortality of only some 20 per cent.

VII. THE RATE OF MORTALITY.

(a) Gross rate of mortality.

Having discussed the period of incubation, let us now turn to the rate of mortality. The following table gives the rate of mortality in the 1,000 cases:—

TABLE IV.

Analysis.	Number of Cases.	Recovered.	Died.	Rate of Mortality per cent.
1914–1917.	1000	594	406	40·6

This rate is, however, too low, since it does not take into consideration the cases which occurred in France, and which were naturally of a severer type than those which occurred in England. Sir WILLIAM LEISHMAN, in his first analysis of cases in France, based upon 179 cases, gives a case mortality of 78·2 per cent. In a second analysis, Major SMALLMAN and he, in 160 cases, gave a case mortality of 73·7 per cent. This would give a total mortality in the 1,339 cases of about 50 cent. The rate of mortality in pre-serum days lay about 85 per cent. Few were expected to recover. In this connection Colonel HARVEY has drawn my attention to a statement in Sir CHARLES BELL'S Diary, written after the battle of Waterloo. He is describing a case of severe tetanus in a soldier belonging to the German Legion. He says, "There are but two cases living of all who had this affection—this man and a French officer. His death was constantly anticipated by all—and by none more than myself—on account of the general ill-success of our means in these cases." This lowering of the death-rate from 85 per cent to 50 per cent. is satisfactory, and is doubtless due in great part to the introduction of the prophylactic inoculation of antitoxin. It must also be borne in

mind that, so far as prophylactic injections are concerned, we were still practically in the pre-serum days during the first months of the war.

(b) The rate of mortality at different periods of the war.

The number of cases of tetanus dealt with at different periods during the war and the rate of mortality are given in table V.

TABLE V.

Analyses.	Number of Cases.	Recovered.	Died.	Rate of Mortality per cent.
1914–15	238	94	144	58·4
1915–16	196	99	97	49·0
Aug. to Oct. 1916	200	127	73	36·5
Oct. to Dec., 1916	100	69	31	31·0
Dec.'16 to Mar.'17	100	81	19	19·0

From this table it will be seen that the fall in the rate of mortality has been progressive. In the first year it was 58·4 per cent., and has since then steadily fallen to 19·0 per cent. in 1917. This result, however we look at it, and to whatever cause it may be due, must be considered as satisfactory.

(c) The position of the wounds in relation to the mortality.

TABLE VI.

Analyses.	Position of Wounds.	Number of Cases.	Recovered.	Died.	Mortality per cent.
1st	Body	45	17	28	62·2
2nd	,,	64	32	32	50·0
3rd	,,	71	48	23	32·4
4th	,,	38	24	14	36·8
5th	,,	30	24	6	20·0
6th	,,	61	51	10	16·3
		309	196	113	36·6
1st	Limbs	193	77	116	60·1
2nd	,,	132	66	66	50·0
3rd	,,	128	79	49	38·3
4th	,,	62	45	17	27·4
5th	,,	70	58	12	17·0
6th	,,	105	73	32	30·4
		690	398	292	42·3

It has sometimes been stated that wounds of the trunk are more liable to be followed by fatal tetanus than wounds of the limbs. From the above table it would appear that the advantage is rather on the side of the trunk—36·6 to 42·3.

(d) The effect of fractures on the rate of mortality in cases of tetanus.

TABLE VII.

Wound.	Number of Cases.	Recovered.	Died.	Mortality per cent.
Fracture ...	348	226	122	35·0
No Fracture ...	652	368	284	43·5

It has also been held that the presence of a fractured bone complicating the wound was a source of danger, and heightened the case mortality. From the above table it will be seen that there is little difference in the rate of mortality in the two classes, but that if there is any advantage it lies on the side of the fractures.

(e) Tetanus occurring after operative interference with the wound.

TABLE VIII.

Number of Cases.	Recovered.	Died.	Case Mortality per cent.
72 (7·2 per cent.)	46	26	36·0

Among the 1,000 cases, 72 are reported to have occurred after operation—a percentage of 7·2. There were 26 deaths—a case mortality of 36 per cent. The Tetanus Committee advise that when operations are performed at the site of wounds, even if they are healed, a prophylactic injection of serum should invariably be given. Among these 72 cases only four are stated to have received this prophylactic injection before the operation, in spite of all recommendations.

(f) On operative interference after tetanus symptoms have appeared.

TABLE IX.

Analyses.	Cases.	Recovered.	Died.	Mortality per cent.
1914–16.	21	11	10	
Aug. to Oct., 1916.	15	11	4	
Oct. to Dec., 1916.	2	2	0	
Dec., 1916 to Mar., 1917.	7	6	1	
Mar. to June, 1917.	8	8	0	
Totals	53	38	15	28·3

The opinion of the Tetanus Committee is that it appears safer to abstain from surgical interference with the wound after tetanus has

supervened. In the 1,000 cases, there were 53 which had such an operation. Of these 38 recovered and 15 died, a case mortality of only 28·3 per cent. From this it would appear that operative interference after tetanus symptoms have appeared, is not the dangerous procedure it has been supposed to be. The rate of mortality, 28·3, compares well with the gross mortality for the 1,000 cases, 40·6 per cent. It must be borne in mind, however, that in many of these cases large curative doses of antitoxin had been given before the operation.

(g) Relation of the number of days which elapse between the date of wound and the onset of symptoms and the rate of mortality.

DIAGRAM VI.

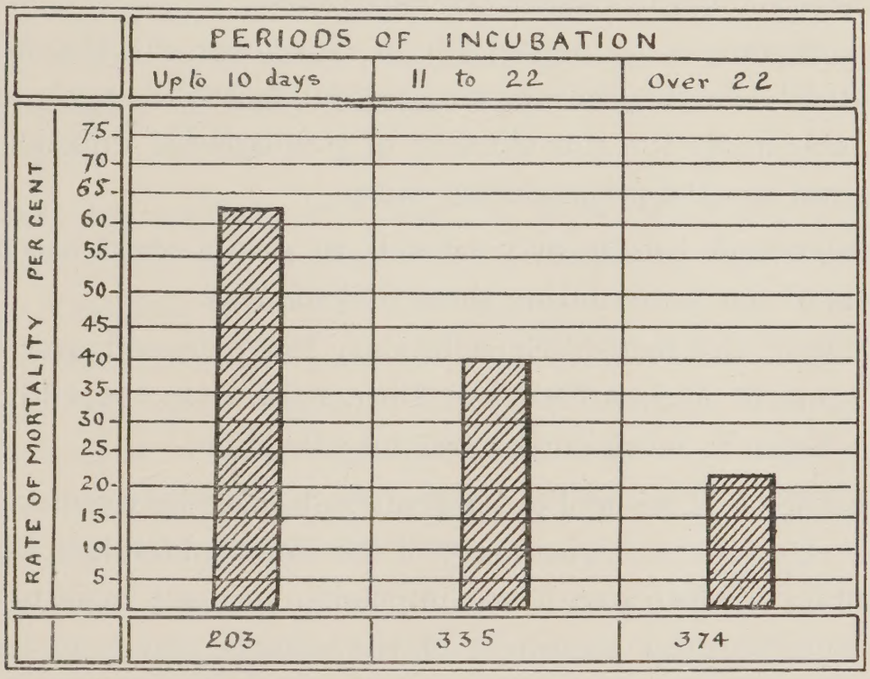


Diagram VI. shews that in the 1,000 cases dealt with, if the symptoms of tetanus appeared within ten days of receiving the wound, the mortality was 63 per cent.; if from the eleventh to the twenty-second day, 40 per cent. The remaining 374 cases with an incubation period of more than 22 days, 22·7 per cent. This is the old story of the longer the period of incubation the lower the rate of mortality.

VIII. TREATMENT OF TETANUS BY ANTITETANIC SERUM.

(A) PROPHYLACTIC OR PREVENTIVE TREATMENT.

I now come to the treatment of tetanus by antitetanic serum, and in the first place let us consider the prophylactic or preventive use of the antitoxin. The first thing in this connection is—

(a) The incidence of tetanus among protected and unprotected soldiers.

Each wounded man receives an injection of 500 units of antitetanic serum as soon after he is wounded as possible. Does this prophylactic injection save a proportion of the inoculated soldiers, or is the incidence alike in the two classes—the protected and the unprotected? When all the data are collected it will be possible to answer this question, but at present it is not permissible. There are no returns available at present of the protected and unprotected populations. That the incidence of tetanus among the wounded is lowered by the prophylactic inoculations seems, however, to be proved by Diagram I. Here it is seen that the ratio of the number of cases of tetanus to the number of wounded is several times as high in September and October as in November. Now to what cause must this marked fall in November and December, 1914, be attributed? No doubt there were several factors at work, but beyond all reasonable doubt the introduction of prophylactic injections of antitetanic serum was the prepondering cause.

To understand this it may be well to give a short account of the movements of our army during these first months.

The bulk of the British Expeditionary Force crossed over to France on the nights of August 12th and 13th, 1914. On the 18th and 19th the troops began to move northwards into Belgium.

The battle of Mons and the retreat took place between August 23rd and 30th. During the retreat many of the wounded fell into the enemy's hands, and on our own part it was impossible in many cases to carry out any thorough surgical treatment of the wounds, owing to the hurried nature of the retreat.

The battle of the Marne was fought between September 7th and 10th.

On September 13th, the British Expeditionary Force reached the valley of the Aisne, and remained here until the end of the month. This was the ground where probably many cases of tetanus were infected. The soil is rich and fertile, and has an evil reputation for tetanus. Here in ordinary times it is found necessary to inoculate the farm horses at intervals with tetanus antitoxin, as an ordinary measure of precaution.

The troops left the valley of the Aisne about October 3rd, and took positions at La Bassée and its neighbourhood, where fighting took place from October 11th to the end of the month.

The severe fighting round Ypres, in which a separate division of the army took part, began on October 20th, and continued until November 11th, 1914.

It is evident then, that the tetanus among the wounded which occurred during September, must have been contracted at the battle of the Marne and in the valley of the Aisne. Further, that the abnormally high ratio of cases of tetanus which is found in October, must have been to some extent due to the tetanised soil of the Aisne valley.

There were therefore several factors at work in September and October, 1914, to raise the ratio—the heavy fighting with the consequent heavy toll of wounded, the highly infective character of the soil, the difficulty of collecting the wounded on account of their numbers and the movements of the troops, and finally the difficulty of giving the thorough surgical treatment to their wounds, which is so essential in the fight against tetanus.

But there was another—and that the most important—factor which has not been taken into account: the prophylactic injection of tetanus antitoxin. This was not carried out during the first two months of the war. It would appear that in the beginning only a small quantity of antitoxin was taken out with the expeditionary force for purposes of treatment, and it was only when the number of cases of tetanus became alarming that steps were taken to ensure that every wounded man should receive a prophylactic dose.

It was not, however, until about the middle of October that prophylactic inoculation was introduced on anything like an adequate scale, and it was at this time that the remarkable fall in the incidence of tetanus took place. A letter received from Sir WILLIAM LEISHMAN, at headquarters in France, corroborates this. He says it was not until the battle of the Aisne that anyone knew what a lot of tetanic infection was going to occur, and the demands for serum increased. Early in October many wounded had not been inoculated, but about the middle of the month the supply sent over became equal to the demand, and its use became practically universal. He concludes by saying that he feels sure that the drop in the incidence of tetanus in November, 1914, was due to the use of the prophylactic dose, and does not think any large complicating factor comes in.

(b) The incubation period in non-protected and protected cases.

Let us now take up the question as to what effect the prophylactic injection has on the incubation period.

We have seen in a previous diagram what the period of incubation is for the 1,000 cases, including protected and unprotected. The following diagrams represent the incubation period in the two classes. There are 201 unprotected and 489 protected among 1,000. Many cases are unrecorded.

DIAGRAM VII.

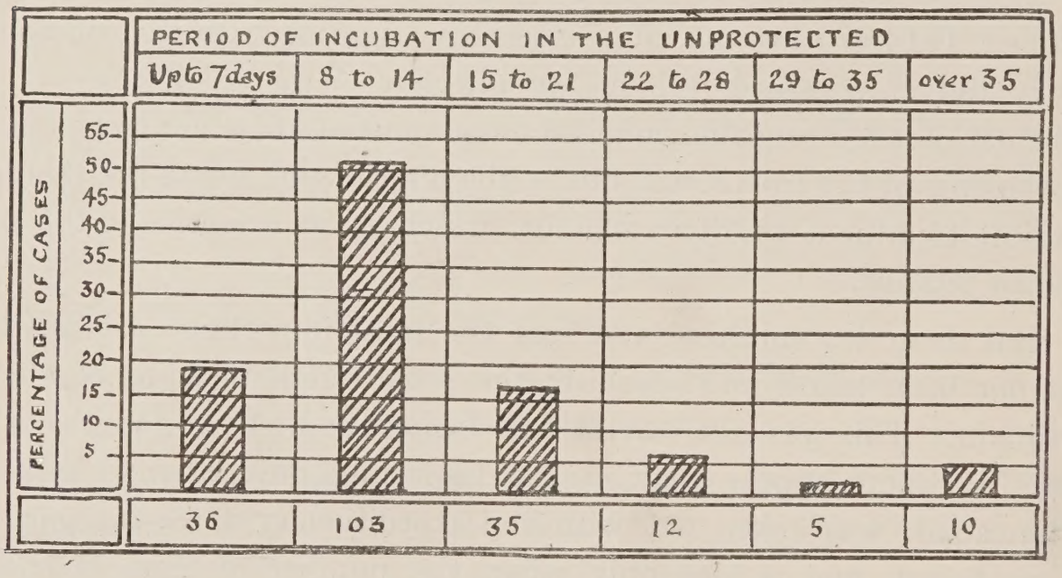
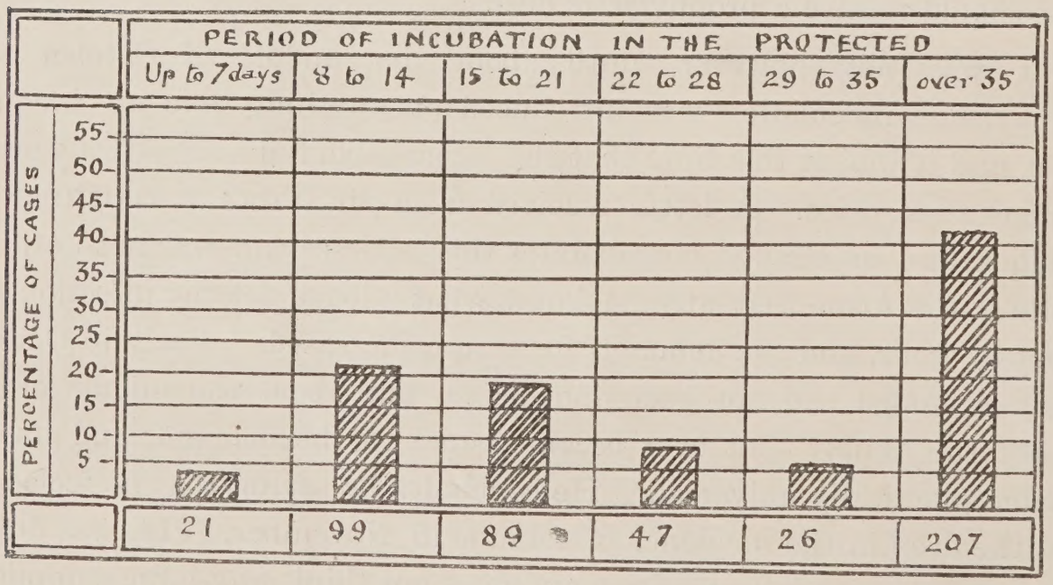


DIAGRAM VIII.



From these two diagrams it will be seen that the incubation period is much lengthened in the protected. Seventy per cent. of the unprotected

cases occur within the first fortnight; only 24 per cent of the protected. Almost half the protected have an incubation period of more than 35 days; only a twentieth among the unprotected. The average incubation period among the protected is 45·0 days; among the unprotected an average period of only 15·2 days.

Of the 201 unprotected cases, 90 recovered with an average incubation period of 18·8 days, and 111 died with an average incubation period of 12·3 days. Of the 489 protected cases, 360 recovered with an average incubation period of 48·75 days, and 128 died with an average incubation period of 34·8 days.

It is, therefore, abundantly manifest that the prophylactic injection of antitoxin lengthens in a marked degree the incubation period.

But I have already shewn that the longer the incubation period the lower the rate of mortality, therefore in this way the prophylactic injections lessen the death-rate. The rate of mortality in pre-serum days, you remember, was 85 per cent. If there had been no prophylactic inoculations in this war we would have lost 850 men in home hospitals alone, whereas we have only lost 406, a saving of 444 men.

(c) The rate of mortality among the unprotected and the protected.

Let us now enquire a little more closely into this question of the rate of mortality among the unprotected and protected. The following table gives the figures:—

TABLE X.

Prophylactic Injections.	Number of Cases.	Recovered.	Died.	Rate of Mortality per cent.
Protected	495	363	132	26·6
Not recorded	266	131	135	50·7
Unprotected	239	100	139	58·1

Among the 1,000 cases under consideration, 495, almost one-half, are noted as having received a prophylactic injection of antitetanic serum. Of these 495 protected cases, 363 recovered and 132 died, giving a mortality of 26·6 per cent. Of the remaining 505 cases there is no record of prophylactic treatment in 266, although in all probability many of them received it. Of these 266 unrecorded cases, 131 recovered and 135 died, a mortality of 50·7 per cent. The remaining 239 cases are stated to have had no prophylactic injection of any kind. Of these, 100 recovered and 139 died, a mortality of 58·1 per cent.

According to these figures the prophylactic inoculation of antitoxin lowers the mortality by more than one-half, namely, from 51·8 per cent. to 26·6 per cent. The two following diagrams also deal with the same subject. They give the rate of mortality in non-protected and protected, arranged in weekly periods according to the period of incubation.

DIAGRAM IX.

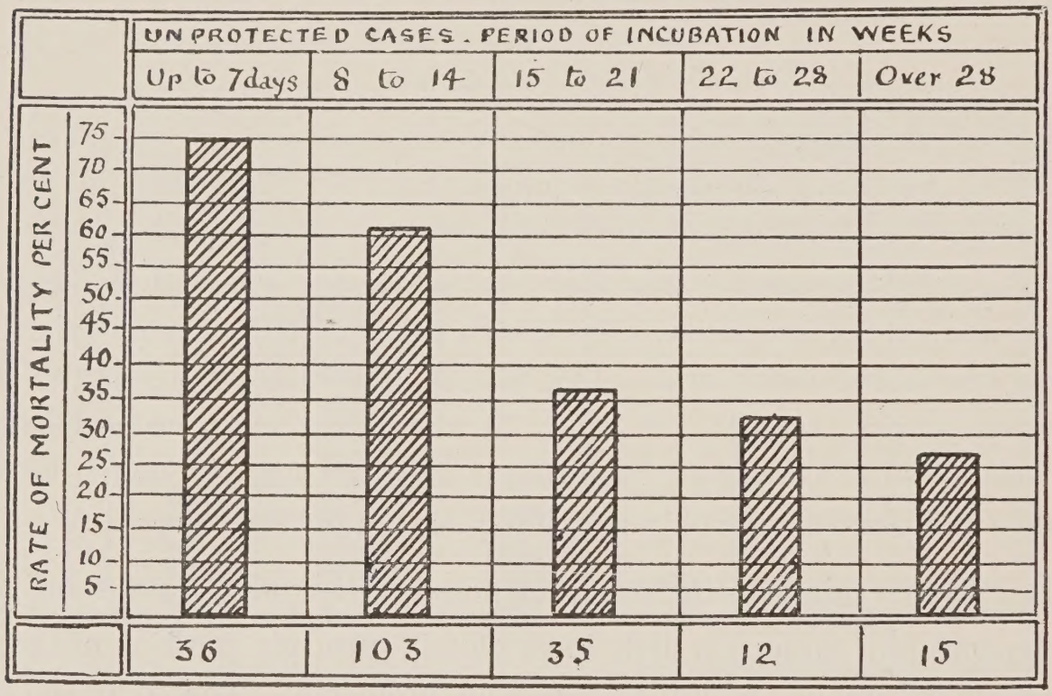
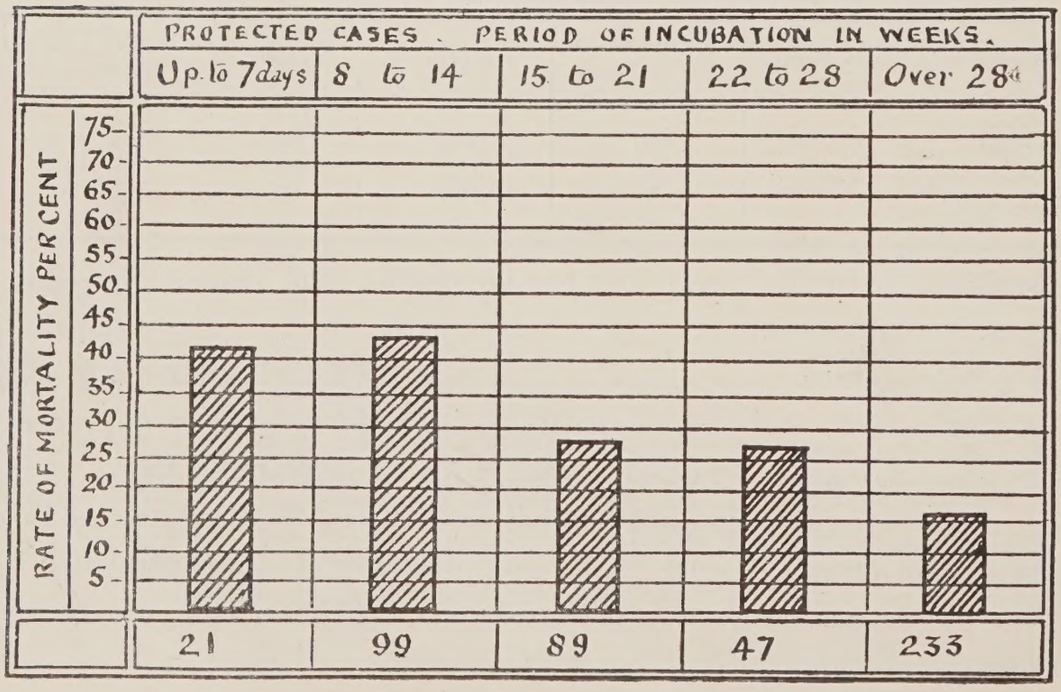


DIAGRAM X.



Among the unprotected cases the mortality is 75 per cent. in those who took the disease within seven days of receiving the wound. Among the protected of the same period the mortality is 42·8 per cent. During the first three weeks 174 cases occur among the unprotected and only 27 after three weeks, whereas among the protected there are only 209 in the first three weeks and 280 after that time.

(d) The effect of one inoculation, or more than one, on the incubation period.

We have seen that the prophylactic inoculation of antitoxin lengthens the period of incubation. The Tetanus Committee have laid down in their latest Memorandum dated June, 1917, that four prophylactic injections should be given to every wounded soldier at intervals of seven days.

DIAGRAM XI.

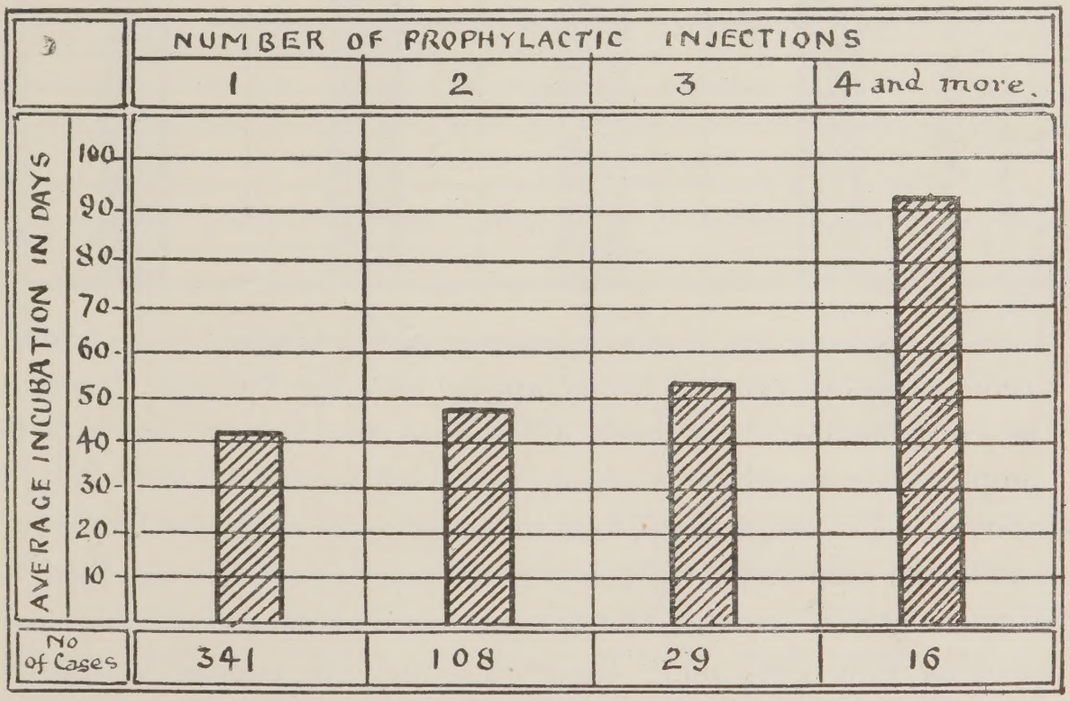
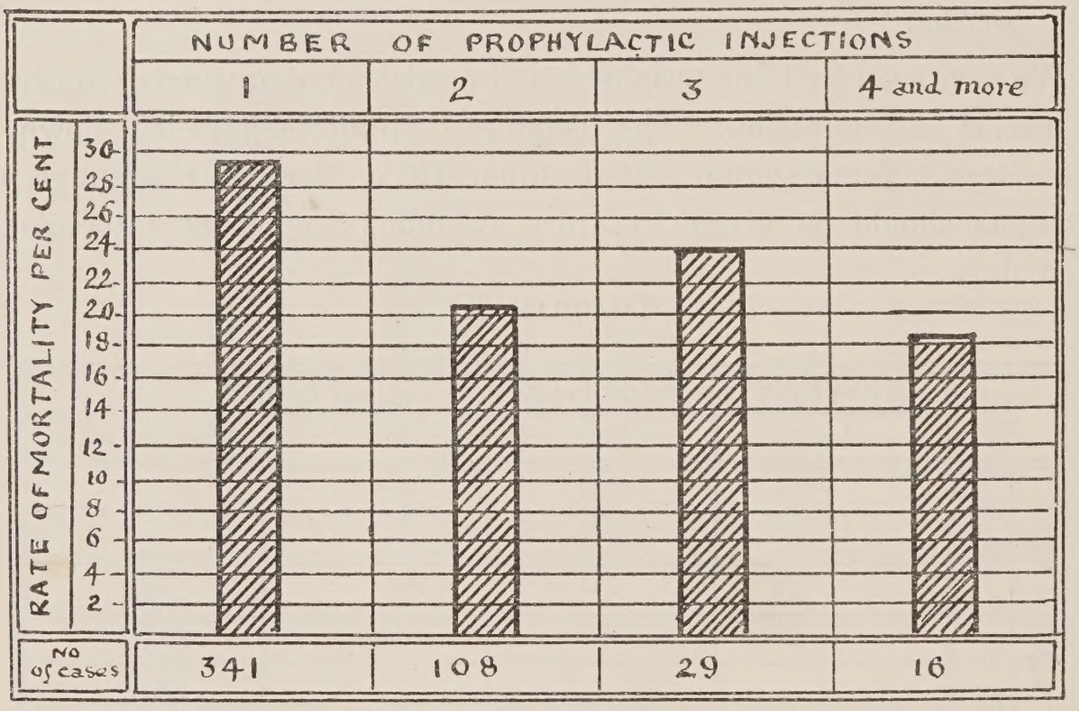


Diagram XI. gives the number of inoculations, the number of cases, and the average incubation periods. From this it will be seen that the inoculation period tends to lengthen as the number of inoculations increases. With one inoculation the average incubation is 40·6 days, with two 47·9 days, with three 53·6 days, and with four or more, 92·6 days.

(e) On the effect of one, or more than one, prophylactic inoculation on the rate of mortality.

The next diagram represents the effect of one, or more than one, prophylactic inoculation on the death-rate. From it it will be seen that wounded men who received one inoculation have a case-mortality of 29·3 per cent.; those who received two, 21·8 per cent.; three, 24·1 per cent.; and four or more, 18·7 per cent.

Diagram XII.



From these diagrams it would appear that the Tetanus Committee may be considered to have been justified in making the new rule that four prophylactic inoculations should be given instead of one. The incubation period is lengthened, and in accordance with the law already mentioned the case-mortality is lessened. The figures for the third and fourth inoculations are still few in number, but this will doubtless be remedied as time goes on. Before leaving the subject it must be confessed that the value of the multiple inoculations is by no means proved by these figures. All that can be said is that there is justification for going on with the experiment until more evidence is accumulated.

(f) What effect, if any, has the time of inoculation on the rate of mortality?

In regard to what influence promptitude in giving these prophylactic inoculations has in reducing mortality, the following table gives all the information which can be drawn from the 1,000 cases.

TABLE XI.

Number of cases.	Inoculated.	Recovered.	Died.	Mortality per cent.
335	On day of wound	243	92	27·46
67	One day after wound ...	52	15	22·38
69	Two days and over ...	54	15	21·7

From this table it would appear that it is better to be inoculated two or more days after receiving the wound than on the day of wound. This seems absurd, but the three rates of mortality do not differ much, and the numbers, 67 and 69, are small. There is also a danger of some fallacy coming in; for example, a man with a slight wound might remain out of hospital for two or more days before he received his prophylactic dose.

(B) THERAPEUTIC OR CURATIVE TREATMENT.

To arrive at a true estimate of the curative value of antitoxin is of the greatest importance, but unfortunately it presents great and, up to the present, insurmountable difficulties. The greatest variety is found in the mildness or gravity of the cases themselves. There are frequent complications, often of the most severe nature. Great variety is found in the method of treatment. Some medical officers swear by large injections of serum by the subcutaneous route, others are equally enthusiastic in regard to the intramuscular, intravenous or intrathecal methods of administration.

Out of the total of 1,000 cases, the number treated with antitetanic serum after the onset of symptoms, was 960. Of these 587 recovered and 373 died, a rate of mortality of 38·8 per cent.

The number untreated was 40; of these 8 recovered and 32 died, a mortality of 80 per cent. These untreated cases mostly occurred at the beginning of the war, so that many did not receive a prophylactic injection, which probably accounts for their high percentage. They reproduce, in fact, the conditions obtaining in pre-serum days.

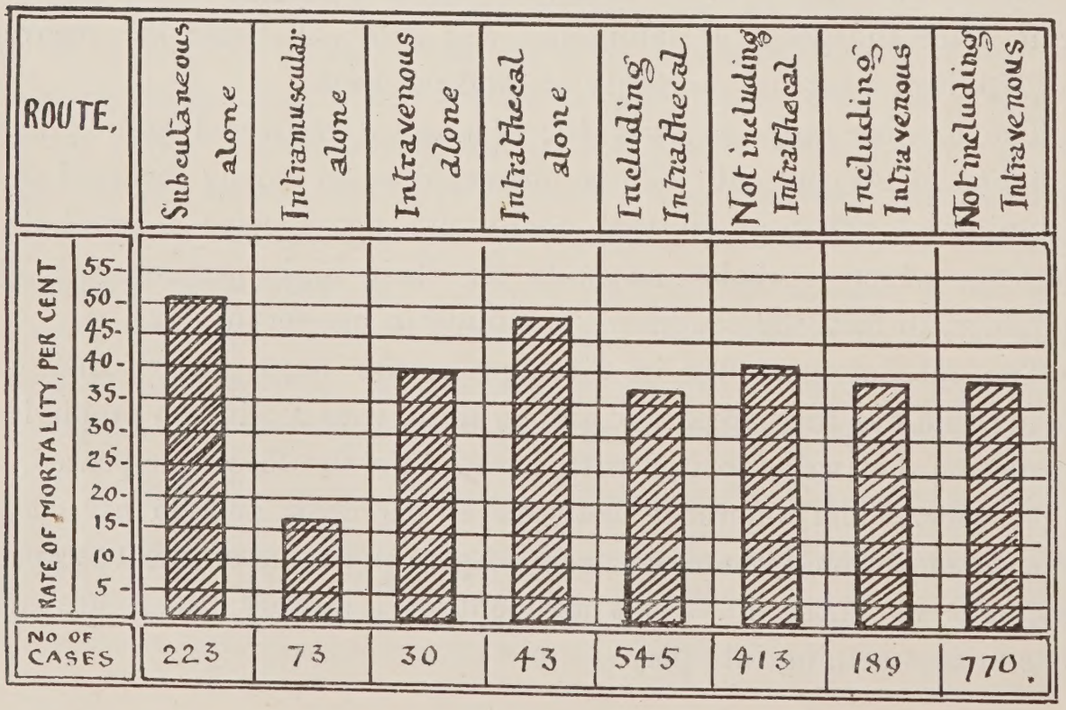
The rate of mortality in these pre-serum days was 85 per cent. During this war the percentage among those who receive no prophylactic inoculation, but were treated with serum after the disease appeared, was 58 per cent. The difference between 58 per cent. and 85 per cent.—27 per cent.—would therefore seem to give the value of the therapeutic treatment by antitoxin. But as mentioned already, there are many other factors coming into play.

(a) On the influence of route in the injection of antitetanic serum.

The Tetanus Committee in their Memorandum are of opinion "that in acute general tetanus the best method of treatment lies in the earliest possible administration of large doses of antitoxin by the intrathecal route." Out of the 1,000 cases—

	Mortality.
223 were treated by subcutaneous injections alone. 110 recovered, 113 died	50·6 per cent.
73 were treated by intramuscular injections alone. 61 recovered, 12 died	16·4 ,,
30 were treated by intravenous injections alone. 18 recovered, 12 died	40·0 ,,
43 were treated by intrathecal injections alone. 22 recovered, 21 died	48·8 ,,
There were 545 cases which included intrathecal injections. 341 recovered, 204 died	37·4 ,,
There were 413 cases which not receive intrathecal injections. 243 recovered, 170 died	41·1 ,,
There were 189 cases which included intravenous injections. 116 recovered, 73 died.	38·6 ,,
There were 770 cases which did not receive intravenous injections. 470 recovered, 300 died	39·0 ,,

DIAGRAM XIII.



It would appear from the diagram that the subcutaneous is the least efficacious and the intramuscular the most. The intravenous seems to have some advantage over the intrathecal. Those cases which included intrathecal injections are no better off, or even rather worse off, than those which did not include intrathecal injections, and the same may be said of the intravenous. But little can be made out of such a diagram. Take, for example, the intramuscular route, which has the lowest death-rate. On examining them in detail, it is found that 22 of them are mild local cases, the rate of mortality of which is nil. Of the remaining 51 cases, 39 recovered and 12 died, a mortality of 23·5 per cent. In regard to the high death-rate after subcutaneous injection, this is probably due to the fact that at the beginning of the war the majority of the cases were treated by this route, many with inadequate doses, and many who had never received a prophylactic dose.

Be this as it may, Professor SHERRINGTON has shewn that, in experimental animals inoculated with a known lethal dose of toxin, the intrathecal route was by far the most efficacious. In the monkeys treated subcutaneously or intramuscularly the disease was hardly retarded in its fatal result, whereas almost all those treated by the intrathecal route recovered. Of course, there is a great difference between tetanus in man and in an experimental monkey. In the former there are living tetanus bacilli; in the latter a weighed quantity of the dead poison. The Tetanus Committee are therefore justified in giving the recommendation quoted above.

(b) Is there any other evidence to be found in the Tetanus Reports that the intrathecal route has any advantage over the other methods of injection?

Treatment beginning on day of onset of disease

	Mortality.
Out of the 1,000 cases 528 cases were treated with antitetanic serum on the day the symptoms declared themselves. 301 recovered, 227 died ...	43·0 per cent.
Out of the 528 cases the following received antitoxin, but not intrathecally, on the day of the disease: 333 cases, 182 recovered, 151 died	45·3 „

Mortality.

Out of the 528 cases the following received antitoxin, including intrathecally, on the day of onset of disease: 195 cases, 119 recovered, 76 died ... ... 38·9 per cent.

Treatment beginning on the day following the onset of disease.

Out of the 1,000 cases 173 cases were treated with antitetanic serum, beginning one day after the symptoms had declared themselves. 103 recovered, 70 died ... ... 40·4 ,,

Out of the 173 cases the following received antitoxin, but not intrathecally, one day after the onset of the disease: 120 cases, 70 recovered, 50 died ... 41·6 ,,

Out of the 173 cases the following received antitoxin, including intrathecally, one day after the onset of the disease: 53 cases, 33 recovered, 20 died ... 37·7 ,,

Treatment beginning two days after the onset of the disease.

Out of the 1,000 cases 89 cases were treated with antitetanic serum, beginning two days after the symptoms had declared themselves. 65 recovered, 24 died ... ... 26·9 ,,

Out of the 89 cases the following received antitoxin, but not intrathecally, two days after the onset of the disease: 42 cases, 32 recovered, 10 died ... 23·8 ,,

Out of the 89 cases the following received antitoxin. including intrathecally, two days after the onset of disease: 47 cases, 33 recovered, 14 died ... 30·0 ,,

Treatment beginning three days and over after the onset of the disease.

Mortality.

Out of the 1,000 cases 143 cases were treated with antitetanic serum three days and over after the symptoms had declared themselves. 110 recovered, 33 died ... ... 23·0 per cent.

Out of the 143 cases the following received antitoxin, but not intrathecally, three days and over after the onset of disease: 71 cases, 57 recovered, 14 died ... 19·7 ,,

Out of the 143 cases the following received antitoxin, including intrathecally, three days and over after the symptoms had declared themselves: 72 cases, 53 recovered, 19 died ... ... 26·4 per cent. Mortality.

Diagram XIV.

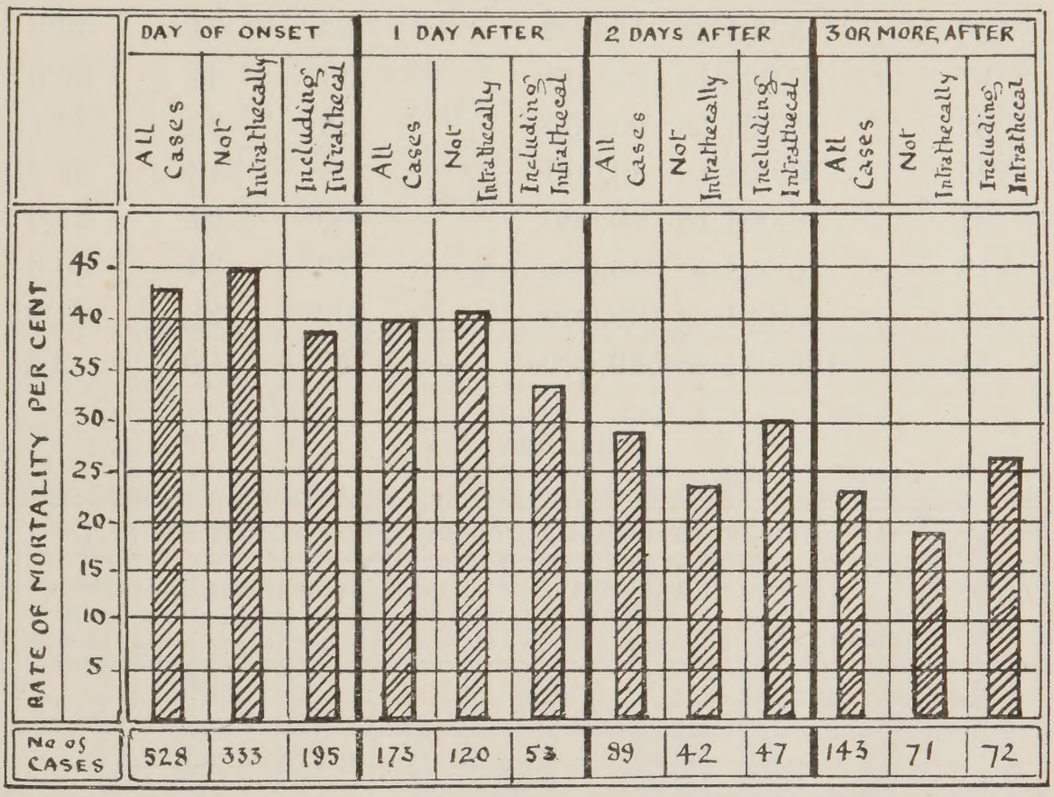


Diagram XIV. represents the result of giving the antitoxin from the day of onset, beginning the treatment one day after the symptoms have appeared, two days after, and three or more days after the onset. You see the slope is downwards. All cases—528 in number—treated from day of onset have a death-rate of 43 per cent.; one day after, 40 per cent.; two days, 27 per cent. This should mean that it is better to defer treatment for some days than to start on the first appearance of tetanic symptoms. But it probably only means that the severe cases are treated at once; the less severe are not diagnosed until some days have elapsed since the appearance of suspicious symptoms, and hence the delay.

It is also evident that no case, either for or against the intrathecal route, can be made out from these figures.

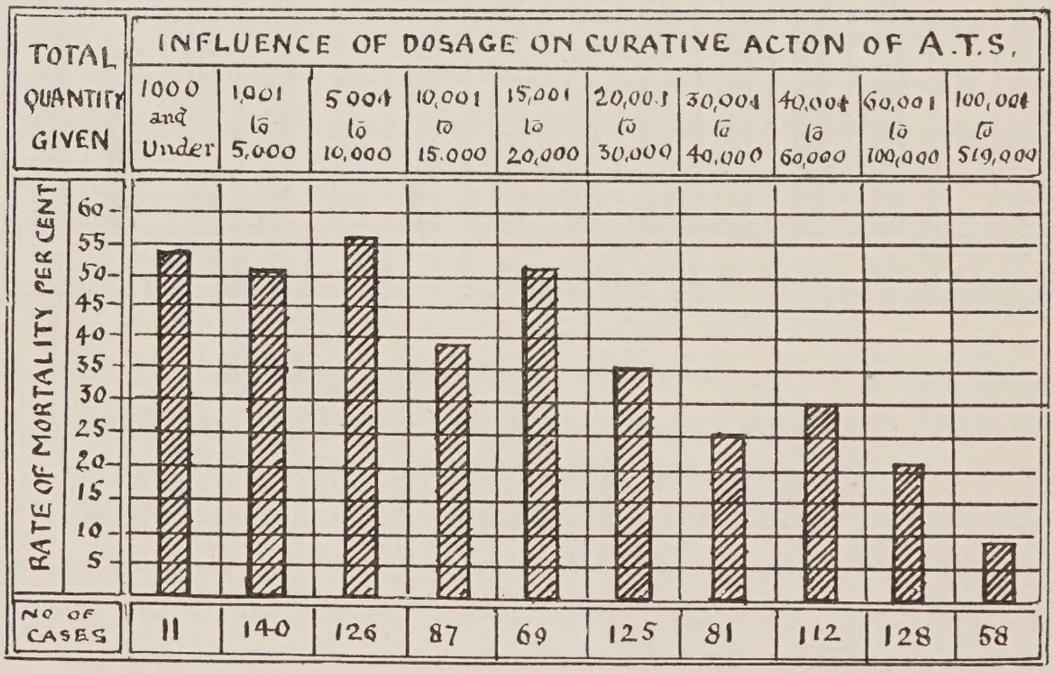
(c) The influence of dosage on the curative action of antitetanic serum.

(1) *The total quantity of antitoxin given during the attack.*

Out of the 1,000 cases:—

				Recovered.	Died.	Mortality.
11	received	1,000 units or under	...	5	6	54·5
140	,,	1,001 to 5,000 units	...	68	72	51·4
126	,,	5,001 to 10,000 ,,	...	55	71	56·3
87	,,	10,001 to 15,000 ,,	...	53	34	39·0
69	,,	15,001 to 20,000 ,,	...	33	36	52·1
125	,,	20,001 to 30,000 ,,	...	76	49	35·2
81	,,	30,001 to 40,000 ,,	...	60	21	25·9
112	,,	40,001 to 60,000 ,,	...	78	34	30·3
128	,,	60,001 to 100,000 ,,	...	100	28	21·9
58	,,	100,001 to 519,500 ,,	...	53	5	9·4

Diagram XV.



It would appear from Diagram XV. that the greater the amount of serum the lower the mortality—277 cases receive 10,000 units and under, with a death-rate of about 55 per cent.; 58 receive from 100,000 to 500,000, with a death-rate of only 8 per cent. The probable fallacy here is that the longer the man lived the more serum he received. The short, acute, early fatal cases had no time to get a large quantity.

(2) *The daily quantity of antitoxin given.*

Out of the 1,000 cases:—

		Recovered.	Died.	Mortality.
29	received 1,000 units or under ...	18	11	37·9
433	„ 1,001 to 5,000 units ...	252	171	40·4
250	„ 5,001 to 10,000 „ ...	175	75	30·0
111	„ 10,001 to 15,000 „ ...	69	42	37·8
68	„ 15,001 to 20,000 „ ...	31	37	54·4
55	„ 20,001 to 30,000 „ ...	26	29	52·7
22	„ 30,001 to 40,000 „ ...	9	13	59·0
9	„ 40,001 to 52,000 „ ...	4	5	55·5

DIAGRAM XVI.

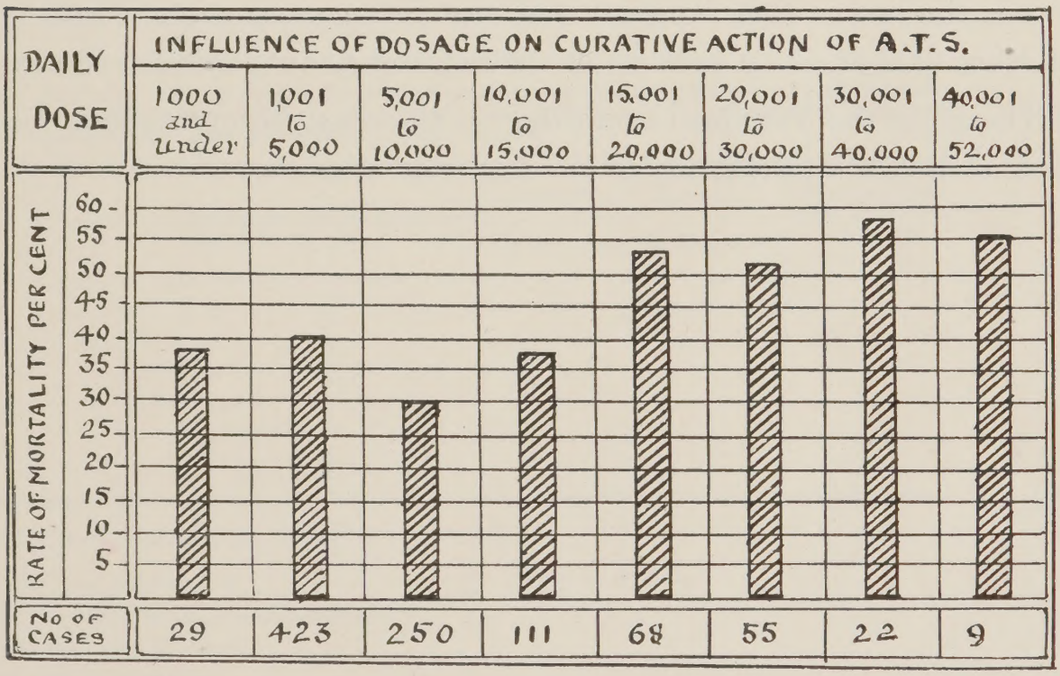


Diagram XVI. gives the daily dose. Here an opposite condition obtains. The larger the dose the higher the mortality. This may be due to the more severe cases being injected with larger daily quantities than the milder cases.

Whatever the reason, it is evident that no useful deductions can be made from these figures.

I said at the beginning of this section on therapeutic treatment, that to arrive at a true estimate of the curative value of antitoxin is of the greatest importance.

It must be confessed that no light is thrown on the question by the figures given.

It is therefore not possible from a study of this analysis to give a dogmatic answer to this question. Perhaps in the course of this discussion some light may be thrown on it.

At present then the position seems to be this: Antitoxin has no power of neutralising toxin fixed in the nervous system. If a fatal amount has been absorbed, then no amount of antitoxin will save the man's life. If there is any free toxin circulating in the blood or lymph, the antitoxin can neutralise it, and so possibly prevent further mischief. If then a fatal amount has not been absorbed the injection of antitoxin may be of use. By animal experiment it is proved that the intrathecal route is the best. It is believed that the intravenous route is also good, but more dangerous on account of the liability to anaphylactic shock.

Therefore the Tetanus Committee, in their last Memorandum, recommend antitoxin intrathecally at the first sign of tetanus.

Army Form W. 3508

REPORT ON A CASE OF TETANUS.

N.B.—To be filled up by the Medical Officer in Charge of the Case, and sent through his Commanding Officer to Surgeon-General Sir David Bruce, A.M.S., Royal Army Medical College, Grosvenor Road, London, S.W.1., immediately after death, or as soon as symptoms of Tetanus have subsided.

Name of Hospital Date of admission to

Name Regtl. No. Rank

Regiment or Corps Age

Date and hour, if possible, of wound

Town or District in which wound was received

Nature and site of wound

How was wound treated in France, etc., before admission to the hospital

PROPHYLACTIC INJECTIONS WITH ANTI-TETANIC SERUM.

N.B.—Entries under this heading relate to injections of serum before symptoms of Tetanus have appeared. These injections should be given, as far as possible, at intervals of seven days.

	Date.	Amount in Units.	Remarks.
First injection—at time of wound			
Evidence. Whether Statement of Patient or Documentary. It should be found on his Field Medical Card, A.F. W. 3118.			
Second injection			
Third injection			
Fourth injection			

TYPE OF CASE.

In order to estimate the value of different methods of treatment it is important to classify the types of Tetanus, as each type has its own rate of mortality.

(*a*) Trismus, the earliest symptom.

1. Tetanus with complete closure of jaws (teeth cannot be separated) developing within 24 hours from onset of symptoms.
2. Tetanus with complete closure of jaws developing after more than 24 hours.
3. With incomplete closure of jaws. Mouth can be partially opened.

(*b*) Trismus, occurring after other symptoms of Tetanus have shown themselves.

(*c*) General Tetanus without Trismus

(*d*) Local Tetanus, without Trismus.

It would be of great service if medical officers would indicate by underlining in ink the type to which they consider their case to belong.

CLINICAL HISTORY.

N.B.—Every officer should take steps to provide himself with a copy of the War Office Memorandum on Tetanus, which can be obtained from his Officer Commanding or D.D.M.S.

CURATIVE TREATMENT WITH ANTI-TETANIC SERUM.

Date and hour of onset of Tetanus symptoms

Put a number opposite each symptom in the order in which it appeared.

Premonitory symptoms

N.B.—In order that trustworthy information may be obtained as to the earliest symptoms of Tetanus, it is most important that officers should pay attention to the accuracy of this record.

(*a*) General.	(*b*) Local
Mental change	Pain
Sleeplessness	Local increase of reflex excitability
Tremors	Sore throat or difficulty in swallowing
Increased reflex excitabilty	Muscular rigidity
	Muscular twitchings

Did Trismus occur at any time during illness?

Was wound foul?

How was it treated?

Operation, if any. Date and nature of

Number of units of Anti-Tetanic Serum injected

N.B.—Date, hour and number of units injected on each occassion to be entered in their respective columns. In the columns "Intravenous" and "Intrathecal" it is important to enter both the number of units and volume in ccm's injected.

Date.	Hour.	Subcutaneous No. of Units	Intramuscular No. of Units.	Intravenous.		Intrathecal.		Distinguishing mark or number on bottle.
				Units	ccm's	Units	ccm's	

Other therapeutic measures, sedatives, etc.

Result: Died or recovered Date of death

Was death the result of Tetanic spasm?

If not, to what was it due?

Accidents due to serum:

1. Anaphylactic shock
2. Serum rash. Nature and severity of

Medical Officer in charge of case.

Date Officer Commanding Hospital.

N.B.—The Officer Commanding should satisfy himself that this Army Form is filled up as fully and accurately as possible.

TETANUS.

INSPECTOR'S REPORT, to be furnished on each case of Tetanus visited. To be sent direct to Surgeon-General Sir D. Bruce, Chairman, Tetanus Committee, Royal Army Medical College. Grosvenor Road, London, S.W.1.

1. Hospital — Date of Visit
2. Patient's Name — Rank — No. — Regt., etc.
3. Date of Wound — Nature and Site of Wound

4. Premonitory Symptoms:— (*a*) Date and Nature of. (*See* Memorandum of Tetanus.) (*b*) Has there been any rigidity of muscles in vicinity of wound? (*c*) What surgical treatment has been employed? (*d*) Was there any surgical interference with wound before or after onset of symptoms?	
5. Prophylactic Injections of Antitetanus Serum:— (*a*) Date, amount and place of Primary Injection in France, if known. (*b*) Date, amount and place of Second Injection. (*c*) ,, ,, ,, Third Injection. (*d*) ,, ,, ,, Further Injections.	
6. Therapeutic Injections of Antitetanic Serum:— (*a*) Date, amount in units and c.cm., and route of injections from day of onset of symptoms to date of visit. (*b*) Was intrathecal injection made on day of onset; if not, why not? (*c*) Was there any serum trouble after first or other injections? If so, what serum was used?	
7. Are notes being taken of the case sufficient to afford data for filling up the Blue Tetanus Form A.F.W. 3508? The Inspector should himself fill up the Form as far as possible on date of visit, and see that the M.O. i/c of case understands the proper mode of filling up the Form.	
8. Are the wounded in this Hospital receiving the Prophylactic Injections of Serum as recommended in Memorandum, and, if not, why not?	
9. Have you any suggestions to make which you think may improve the treatment of cases of Tetanus, and reduce the mortality?	

TYPE OF CASE.

In order to estimate the value of different methods of treatment it is important to classify the types of tetanus, as each type has its own rate of mortality.

A. Trismus initial symptom.

1. Tetanus with complete closure of jaws (teeth cannot be separated), developing within 24 hours from onset of symptoms.
2. Tetanus with complete closure of jaws, developing in more than 24 hours.
3. With incomplete closure of jaws. Mouth can be partially opened.

B. Trismus occurring after other symptoms of tetanus have shown themselves.

C. Local tetanus, without trismus.

CLINICAL HISTORY.

....Inspector of Tetanus.

Date..... ....

Memorandum on Tetanus.

(THIRD EDITION.)

This Memorandum on the prophylaxis and treatment of tetanus has been drawn up with the authority of the War Office by the War Office Committee for the Study of Tetanus, and is to a great extent based on experimental and clinical evidence which has become available since the beginning of the present war.

It is divided into the following sections:—

I.—Prophylactic or preventive treatment of Tetanus.
II.—Dosage in prophylactic or preventive treatment of Tetanus.
III.—Precautions to be taken before operating on wounds.
IV.—Antiseptics which may be of use in the preventive treatment of Tetanus.
V.—Diagnosis.
VI.—Therapeutic or curative treatment of Tetanus.
VII.—Dosage in the therapeutic or curative treatment of Tetanus.
VIII.—Anaphylaxis.
IX.—Surgical treatment of the wound after Tetanus has appeared.
X.—Supply of Antitetanic Serum.
XI.—Instructions to Inspectors of Tetanus.
XII.—Instructions to Officers in charge of hospitals.
XIII.—Instructions to Medical Officers in charge of wounded.
XIV.—Appendix A. Method of performing an intrathecal injection.
XV.—Appendix B. List of papers published by the Tetanus Committee.

The Memorandum was first issued in August, 1916, and a revised edition in October of the same year; but as a good many questions have since arisen in regard to various points, it has been thought advisable to issue a third edition.

A question, for example, has arisen as to whether this Memorandum is to be looked upon as an Army Order or as a number of suggestions which may or may not be carried out, according to the inclination or judgment of the officers in charge of hospitals. In answer to this it may be stated that, in so far as it concerns the prophylactic or preventive treatment the Memorandum should be regarded in the former sense; and in so far as it concerns the therapeutic or curative treatment in the latter sense. It has never been the policy of the Army Medical Authorities to interfere with the treatment of the sick soldier by his Medical Officer. With regard to prophylaxis, on the contrary, whether of small-pox, typhoid fever, or tetanus, it is an Army Order which must be carried out, whatever the personal predilections of the Medical Officers in charge of hospitals may be. In order to make this plain an Army Council Instruction, No. 2436, was issued in 1916.

I.—THE PROPHYLACTIC OR PREVENTIVE TREATMENT OF TETANUS.

The prophylactic value of injections of antitetanic serum is beyond all doubt, but there is strong experimental evidence that in about ten days the immunity conferred by an injection is, to a great extent, lost.

It is impossible, from the appearance of any wound, to determine whether it is infected with tetanus bacilli or not; and whereas many cases of tetanus have occurred not only in men with healed wounds, but also in those whose wounds were from the beginning practically clean, it has been decided that all wounded men shall receive at least four injections of antitetanic serum; that is to say, a primary injection given at the time of the wound and three others.

It is, therefore, essential that a second, third and fourth subcutaneous injection should be given to all wounded men, and in order to anticipate the total disappearance of antitoxin from the body, the second injection should follow the first at an interval of seven days, or as soon after this as possible. The third and fourth injections must also follow at the same interval of time.

As many cases of tetanus have occurred in men suffering from trench feet, sometimes without obvious breach of surface, these cases must be treated as wounded men.

II.—DOSAGE IN PROPHYLACTIC OR PREVENTIVE TREATMENT OF TETANUS.

It may be definitely stated that the danger of anaphylactic shock is negligible when prophylactic doses of 500 U.S.A. units contained in 3 per cent. or less of horse serum, are

given subcutaneously. This holds good however long the interval between the injections may be. There may be sometimes a serum rash.

The primary injection, given at the front, consists of 500 U.S.A. units, and the second, third and fourth injections should be of the same amount.

The primary injection is given as a rule at the Dressing Station of a Field Ambulance, as soon as the wounded soldier is removed from the firing line. The second and following injections will most frequently be given at Home Hospitals, and sometimes injections will have to be given at Auxiliary Hospitals. The ordinary phial usually contains 1,500 units of tetanus antitoxin. One-third of a phial should, therefore, be injected into each wounded man. Phials containing a single dose of 500 units are also now available. There is no necessity to sterilise the syringe after each injection, as the serum is aseptic and, moreover, contains an antiseptic; it will be sufficient if a freshly sterilised needle be used for each case.

It is hardly necessary to add that care should be taken to ensure that the skin and needle are both sterilised, as neglect of this precaution is apt to lead to abscess formation.

III.—PRECAUTIONS TO BE TAKEN BEFORE OPERATING ON WOUNDS.

When operations are performed at the site of wounds, even if they are healed, a prophylactic injection of serum should invariably be given if the operation be performed at a greater interval than seven days from the last injection.

This precaution is very necessary, as numerous cases have occurred in which the performance of a simple operation has been followed by an attack of tetanus, although in many cases the primary wound had been healed several weeks before the operation.

This precautionary injection may consist of a single subcutaneous injection of the ordinary prophylactic dose of 500 units, or a larger dose may be injected if it be thought advisable.

It is better to give it two days before the operation, as it takes some 48 hours for the antitoxin to be fully absorbed after subcutaneous injection. Injected intramuscularly the absorption is quicker—probably in about 12 hours—so that this method could be used if time were pressing.

IV.—ANTISEPTICS WHICH MAY BE OF USE IN THE PREVENTIVE TREATMENT OF TETANUS.

The group of oxidising antiseptics, such as hydrogen peroxide, potassium permanganate, chlorine water, Dakin's solution, and solution of iodine, are particularly unfavourable to the anaerobic growth of the tetanus bacilli. They have also the power of rendering toxin non-toxic.

V.—DIAGNOSIS.

The classical symptoms of tetanus, as described in the majority of the text books, refer to a phase of the disease in which treatment will have lost much of its power and value. With many medical men, tetanus is not tetanus until the symptoms of *risus sardonicus* and lockjaw are present.

In those who have been partially protected by a prophylactic injection of antitoxin, trismus and general symptoms may not occur at all, or not until late in the disease, possibly not until months have elapsed. This is known as delayed tetanus. In such cases the manifestations of tetanus may be confined to local spastic rigidity of the wounded limb, which may persist for weeks or months and then disappear; or may develop into generalised tetanus. This so-called localised tetanus is a distinct and not infrequent type of the disease and should be carefully watched for.

The early diagnosis of tetanus is of the greatest importance. All clinical and experimental evidence tends to show that the chances of successful treatment diminish rapidly as the length of time increases after the first symptoms have been observed.

Tetanus toxin reaches the motor nerve cells of the central nervous system by travelling up the nerves; it is not directly conveyed to the nerve cells by the blood. In a large number of cases the toxin appears to reach the spinal cord primarily by the nerves which are in connection with the seat of the injury, and, therefore, the motor nerve cells governing the muscles around the wound will be the earliest affected, such affection showing itself in the form of spasticity and increased reflex excitability from these muscles. The patient may complain of jerking or jumping, or stiffness in the affected limb, occurring especially at night. In some cases these symptoms may precede the other symptoms of tetanus by many hours or days. It is, therefore, desirable that the muscles in the vicinity of the

wound should be examined whenever dressings are removed, and the occurrence of rigidity or twitchings, or of local increased reflex response to gentle tapping or pressure, should be immediately reported to the surgeon in charge.

All nursing sisters engaged in dressing wounds, should be warned to give the alarm if the muscles round the wound should be harder or more rigid than the muscles of the uninjured limb or side.

In other cases tetanus toxin is absorbed from the wound into the blood stream and reaches the central nervous system by way of nerves other than those in direct anatomical continuity with the wound, and, hence, early symptoms may sometimes be observed in muscles supplied by any motor segment of the cord or brain.

The muscles supplied by the fifth nerve are those most commonly affected, as is shown by the occurrence of trismus as an early symptom. In a wounded man this symptom should be taken as a decisive indication of tetanus in the absence of any other obvious source of reflex spasm. Other cranial nerve symptoms may be facial spasm or paralysis, or paralysis or spasm of the eye muscles with consequent strabismus.

Spasm of the pharyngeal muscles may also occur, which is often complained of by the patient as sore throat, and occasionally causes reflex yawning. The tongue muscles may be affected, causing deviation of the tongue when protruded. Tetanic spasm of the neck muscles may be complained of as stiff neck. Spasm of the thoracic and abdominal muscles is an occasional early symptom, often giving rise to complaints of stitch in the side or to difficulty in micturition.

Often before the onset of any definite symptom of tetanus there is a general increase of muscular tone, and the deep reflexes are exaggerated; knee and ankle clonus may be produced in the absence of any signs pointing to the involvement of the pyramidal tract, such as an extensor plantar response or loss of the abdominal reflexes.

The general increase of tone is manifested in the facial muscles by the drawn expression of the patient, and the increased reflex excitability often leads to psychical irritability and insomnia.

The occurrence of a generalised tetanic toxaemia may be marked by profuse local or generalised sweating.

Once the diagnosis of tetanus has been definitely established, the patient should be examined as little as possible.

It is very desirable to obtain the co-operation of Medical Officers in the endeavour of the Committee to formulate the early symptomatology of this disease, and therefore confirmation of, or any addition to, the above will be welcomed.

Any brief account of early symptoms observed, either in the major or in the minor forms of the disease, will be of great value, and officers are requested to forward any such observations to Surgeon-General Sir David Bruce, Chairman of the Tetanus Committee, at the Royal Army Medical College, Grosvenor Road, London, S.W. 1.

VI.—THERAPEUTIC OR CURATIVE TREATMENT OF TETANUS.

It cannot be too strongly emphasised that time is the all-important element in the treatment of tetanus. As short a time as possible should be allowed to elapse between the diagnosis and the commencement of active treatment. A delay of an hour may make all the difference between success and failure.

It is on this account that the early symptoms are of the greatest importance. In almost every case of tetanus in those who have received a prophylactic dose of antitoxin there are found local manifestations of the disease, very often hardness and rigidity of the muscles round the wound, and these signs can be seen or felt for days or even weeks before the occurrence of trismus. In a case on record, these local symptoms had been present for three weeks before the trismus showed itself and before tetanus was suspected. One Medical Officer is reported to have said that symptoms of tetanus were present in a case but were not sufficiently severe to justify the use of antitoxin. According to present ideas it should no longer be permissible to wait for the occurrence of lock-jaw before deciding that the case is tetanus; 5,000 units of antitoxin serum are of more avail at the very beginning, when the disease is still localised, than 50,000 when the symptoms have become general. The moment, then, that any local manifestation of tetanus is observed, it is recommended to proceed at once to vigorous specific treatment. It is even more urgent to act on the earliest manifestation of trismus without waiting for the appearance of other signs of tetanus.

The treatment of tetanus may be divided into specific and symptomatic.

1. Specific.—Specific treatment consists in the giving of tetanus antitoxin, which has the power of neutralising the tetanus toxin with which it comes in contact. The problem in treatment is to bring about this contact in the fullest and speediest manner. There are four methods which are commonly employed for the administration of antitoxin:—

(a) *Subcutaneous.*—In this method the serum is injected beneath the skin, from whence is is slowly absorbed into the circulation; it has been determined that some 48 hours elapse before the maximum concentration in the blood is reached. This slowness of absorption is an advantage when it is desired that the action of the serum should be prolonged, as in prophylactic administration. But it is a grave disadvantage when quickness of action is all-important, as in acute tetanus; in such a case little can be expected from this method at the beginning of treatment, although it is useful later in order to keep up the antitoxic action

(b) *Intramuscular.*—Here the serum is injected into the muscles, from which it is absorbed into the circulation more rapidly than from the subcutaneous tissues. It is therefore, as regards speed, better than the subcutaneous method; nevertheless, it must be remembered that full absorption, even here, takes 12 or more hours.

(c) *Intravenous.*—Here the serum is injected directly into the blood stream and immediately diffused throughout the body in such a way as to neutralise all circulating toxin. This is the most rapid route by which the neutralisation of circulating toxin can be accomplished. The objection to this method is that large doses of serum introduced into the circulation, in persons who have previously had an injection, are apt to bring about anaphylactic shock, which may prove fatal. Intravenous injection is therefore not recommended except in cases where the intrathecal method is, for any reason, impossible.

(d) *Intrathecal.*—Here the serum is introduced by lumbar puncture into the sub-arachnoid space of the spinal canal. It soon begins to escape into the blood stream, so that the neutralisation of circulating toxin is quickly effected.

The Committee is of opinion that in Acute General Tetanus the best method of treatment lies in the earliest possible administration of large doses of antitoxic serum by the intrathecal route, repeated on two, three or four days in succession, and combined, if thought desirable, with intramuscular injections.

The introduction of the serum into the sub-arachnoid space always produces turbidity of the cerebro-spinal fluid, due to polymorphonuclear leucocytosis; this reaction is sometimes associated with transient symptoms of meningeal irritation, which need cause no alarm. With ordinary precautions the risk of septic infection is negligible.

In the *chronic form of tetanus,* particularly the form of localised tetanus limited to one limb, without trismus or other sign of generalisation, there appears to be no need to resort to intrathecal injection. A course of serum treatment by the intramuscular method will, in most cases, do all that is required.

VII.—DOSAGE IN THE THERAPEUTIC OR CURATIVE TREATMENT OF TETANUS.

Experience has shown that in the treatment of acute general tetanus the best results are obtained from very large doses of serum; the more acute the case the larger should be the doses of serum employed. The object is to saturate the body with antitoxin as quickly as possible and to maintain the saturation. For this purpose from 50,000 *to* 100,000 *units may be given during the first few days of treatment.*

Tetanus antitoxin is issued to military hospitals in two strengths. The weaker is put up in phials containing either 500 or 1,500 units, the more concentrated in phials containing 8,000 units. Every general hospital should have in stock a supply of the high potency serum in order that there may be no delay should a case of acute tetanus occur in the district. This high potency serum should always be employed for intrathecal injections, because this route differs from the others in the fact that the amount of fluid which can be introduced is limited. This high potency serum should be reserved for intrathecal injections alone.

The amount of cerebro-spinal fluid which can be withdrawn on lumbar puncture will not, as a rule, be more than 20 ccm. It is usually held to be undesirable to run in more serum than will replace the cerebro-spinal fluid drawn off, and in cases where little or no fluid can be withdrawn it is not wise to inject more than 20 ccm. of serum, *and this very slowly.* The 16,000 units, contained in two phials, of the high potency serum is an adequate single dose for intrathecal injection. It may be supplemented by intramuscular or subcutaneous injection.

The intrathecal injections may be repeated daily for three or four days, together with supplementary doses by other routes. When the disease shows distinct signs of abating the dose may be decreased, the interval between the doses lengthened and the serum given only subcutaneously.

The following outline of the successful treatment of a case may be given as an example of serum treatment in early acute tetanus:—

Day.	Subcutaneous.	Intramuscular.	Intrathecal.
1st day	—	8000	16000
2nd day	—	8000	16000
3rd day	—	4000	8000
4th day	—	4000	8000
5th day	2000	—	—
6th day	2000	—	—
7th day	2000	—	—

In local tetanus, without implication of the higher centres, doses of 3,000 to 6,000 units may be given daily by the intramuscular or subcutaneous routes. But if in such cases the disease shows signs of extending to the higher centres, it is recommended to give at least one full dose by the intrathecal route.

2. Symptomatic.—Symptomatic treatment consists in the exhibition of sedative drugs. Morphia may be given in $\frac{1}{4}$-grain doses and administered every four hours; some prefer full doses of chloral hydrate; potassium bromide, chloretone, or paraldehyde may also be given by the mouth or rectum.

Carbolic acid.—There is no convincing evidence that the carbolic acid treatment of tetanus has any curative effect whatever, or any action upon the course of the disease It is not recommended.

Magnesium sulphate.—Treatment by sulphate of magnesium has no effect upon the disease itself. The cessation of spasm which follows an injection is only temporary, and is purchased at the cost of risks which are far from negligible. It is very doubtful if any real advantage is gained by its use. It is not recommended.

VIII —ANAPHYLAXIS.

The War Office have issued a "Memorandum on the Use of Curative Sera," which discusses anaphylactic shock, its causes and treatment. This memorandum should be consulted by Medical Officers before treating cases of tetanus. Copies can be obtained from the D.D.M.S. in the different Commands, or from A.M.D. 2, War Office.

IX.—SURGICAL TREATMENT OF THE WOUND AFTER TETANUS HAS APPEARED.

There is a general impression that it is of advantage to excise the wound, or amputate the limb in cases of tetanus. The matter is one upon which there is considerable difference of opinion. From the clinical experience of many observers it would seem that these procedures are of little avail and may actually accelerate the cause of the disease. Animal experiment, so far as it goes, also suggests that operative measures are useless.

While more evidence is required before any dogmatic statement can be made, it appears to be safer to abstain from surgical interference with the wound until the ordinary treatment for tetanus has been carried out, unless there exist other and imperative reasons for immediate operation.

When the symptoms of tetanus have subsided and the tissues are flooded with antitoxin, then the wound can be opened up and searched for foreign bodies or hidden collections of pus and tetanus bacilli.

X.—SUPPLY OF ANTITETANIC SERUM OR ANTITOXIN.

The country generally has been divided into areas of about 10 miles radius, in each of which areas a central hospital acts as a distributing centre for serum so that it

can issue to any of the hospitals in its area, without any delay, a sufficient supply of serum to begin the treatment of a case of tetanus. The Distributing Centre indents on the General Hospital of its Command for adequate supplies of serum for prophylactic and curative purposes. Serum should be stored in as cool a place as possible.

XI.—INSTRUCTIONS TO INSPECTORS OF TETANUS.

In every Command one or more officers with special knowledge should be detailed by the D.D.M.S. to visit cases of tetanus and to assist when necessary in their treatment. These officers should be at the general hospitals of the district, and their names and telephonic addresses should be communicated to the officers and medical practitioners in charge of auxiliary and V.A.D. hospitals.

The working out of a scheme for the supply of serum and syringes to these subsidiary hospitals is a duty which devolves on the Inspector of Tetanus.

On the occurrence of a case of tetanus the Inspector will be immediately informed, and he will at once proceed to visit the case and offer assistance in the carrying out of such treatment as has been suggested in the present memorandum.

He will if necessary assist in the operation of lumbar puncture and intrathecal injection. This will seldom be necessary, as, from what has already been said as to the danger of even an hour's delay, this intrathecal injection will usually have been given before his arrival.

He will make careful inquiry into the case in order to ascertain if any early symptoms had been present and had escaped notice. He will note what prophylactic injections have been made, and if omitted, will ascertain why they were omitted.

When visiting the hospital where the case has occurred he will ascertain if the other wounded men are receiving prophylactic injections.

He should see that sufficient notes of the case are being kept in order that the Tetanus Form can be filled up as fully as possible. For example, it is very seldom that the distinguishing marks on the bottles of serum are reported. This should be done because if serum trouble arises it is evident that this information is essential.

He will forward an Inspector's Report to Surgeon-General Sir David Bruce, with as little delay as possible.

The ordinary Tetanus Report, A.F. W3508, will be filled in by the medical officer in charge of the case. Too great care cannot be taken in this matter of the reports, as the value of any analysis made from them depends on their accuracy and completeness.

XII.—INSTRUCTIONS TO OFFICERS IN CHARGE OF HOSPITALS.

Officers in charge of hospitals will be responsible for the administration of the second, third and fourth prophylactic doses of antitoxin to all wounded under their care, unless grave reasons exist for withholding them. The administration of antitoxin will be recorded on the soldier's Field Medical Card (*A.F. W*3118).

The Officer in charge of a hospital will satisfy himself that each medical officer in his hospital has a copy of the "Memorandum on Tetanus," and that each sister, nurse or dresser of wounds has a copy of the "Notes on the Nursing of Tetanus." He will impress upon medical officers and nurses the paramount importance of early detection of symptoms and early specific treatment.

He will satisfy himself that the proper instruments and an adequate supply of antitoxin are ready to hand, or within easy reach, in order that no delay may take place in beginning treatment. As soon as a case of tetanus is reported to him, he will immediately inform the Inspector of Tetanus, by messenger, telephone or telegram.

When patients are transferred from one hospital to another the number of injections given, with dates, must be entered on his Field Medical Card.

This is the best document on which to record the prophylactic injections. It comes with the wounded soldier from overseas and accompanies him wherever he goes, as long as he remains in any hospital; that is, until he is discharged to duty or is invalided out of the service. By this means a complete history of his prophylactic serum treatment will be available in case the wounded man develops tetanus, and it will be possible in time to estimate the effect of the second, third and fourth injections.

Medical Officers in charge of hospitals will, as heretofore, inform Surgeon-General Sir David Bruce, by telegram, of the occurrence of a case of tetanus, giving the number, name, rank and regiment, and on the recovery or death of the case forward

the usual Tetanus Report to him, in accordance with War Office instructions. If the case recovers, this report, A.F. W3508, should be sent in as soon as the tetanus symptoms have subsided; it should not be kept back until the patient's discharge from hospital, as is often the case.

Any abnormalities of behaviour of antitetanic serum should be carefully observed and reported.

As the Tetanus Committee was appointed for the purpose of studying tetanus, it is greatly to be desired that every medical officer will co-operate in a collective investigation, and submit any evidence in his possession which may add to our knowledge of the disease and its treatment.

XIII.—INSTRUCTIONS TO MEDICAL OFFICERS IN CHARGE OF WOUNDED.

Every medical officer in charge of wounded will make himself acquainted with the contents of the Memorandum on Tetanus, No. 4779, A.M.D. 2, issued by the War Office, and will see that every nurse under him has a copy of the "Notes on the Nursing of Tetanus," also issued by the War Office, and will satisfy himself that she is fully aware of the importance of reporting early symptoms to the nearest available medical officer.

He will be responsible for the carrying out of the recommendations of the Tetanus Committee in regard to the prophylactic injection of all wounded under his care, bearing in mind that cases of trench feet are especially dangerous.

Information regarding previous prophylactic injections will be obtained from the soldier's Field Medical Card, A.F. W3118.

As soon as tetanus is suspected, he will at once take steps to have the patient removed to a special ward, where light and sound can be excluded, and placed under the care of a thoroughly trustworthy and sympathetic sister.

The importance of such nursing details, as the protection of the patient from every kind of external stimulus, cannot be too strongly emphasised.

He will report the case to the Medical Officer in charge of the hospital. If the tetanus is generalised as shown by trismus and other symptoms, he should proceed at once to carry out serum treatment in accordance with the recommendations given in the section on Curative treatment, without waiting for the Tetanus Inspector.

He is especially requested to keep careful notes on the Case Sheet of the symptoms and progress of the case in order that as full and complete a Report as possible may be rendered on A.F. W3508.

War Office, S.W.
June, 1917.

XIV.—APPENDIX A.

The Method of Performing an Intrathecal Injection.

The patient should preferably be under general anæsthesia. The skin over the area of the fourth and fifth lumbar spines should be painted with iodine or cleansed with soap and water followed by an antiseptic. A spinal needle and syringe, or, if the gravity method be used, the usual indiarubber tubing, should be boiled in normal saline, *and the surgeon must observe throughout the most rigorous aseptic precautions.*

The patient is bent head to knees, so as to present as fully a curved back to the operator as possible, and the position of the fourth lumbar spine ascertained by drawing an imaginary line between the highest points of the crests of the ilia.

The tip of the finger is placed on the supraspinous ligament connecting the summits of the spinous processes of the fourth and fifth lumbar vertebrae. The needle is inserted about three-eighths of an inch to one side of the middle line and directed forwards and slightly upwards and inwards. If the needle strikes the bone it should be withdrawn and a fresh attempt made. The canal is reached at a depth, on an average, of about 2½ inches. The trochar is withdrawn and about 20 ccm. of cerebrospinal fluid allowed to flow out into a measured vessel. The syringe is then fitted to the needle and the serum injected. Many surgeons prefer to run in the serum by gravity, and this is undoubtedly a good method. It is hoped to supply high-potency serum in glass tubes drawn out at each end, so as to make this method easier of application by those officers who desire to use it.

It is important that the serum be heated to the temperature of the body and that the injection be made very slowly.

The canal can also be reached by pushing the needle through the supraspinous ligament in the middle line halfway between the two spinous processes.

If several injections have to be made, it is well to choose fresh sites.

Blocking of the flow of the cerebrospinal fluid by a blood clot may be overcome by reinserting and withdrawing the trochar.

The bed should be tilted at the foot and the pillow removed for an hour or two after the injections.

XV.—APPENDIX B.

List of papers written by members of the Tetanus Committee, and others, which may be consulted.

"Memorandum on the Use of Curative Sera." Issued by A.M.D. 2, War Office, 1917.

"Notes on the Nursing of Tetanus." Issued by A.M.D. 2, War Office, 1917.

"On the Intrathecal Route for the Administration of Tetanus Antitoxin." By Major F. W. Andrewes. *The Lancet*, May 5, 1917.

"An Analysis of Cases of Tetanus Treated in Home Military Hospitals from August, 1914, to August, 1915." By Surg.-General Sir David Bruce. *The Lancet*, October 23, 1915.

"An Analysis of Cases of Tetanus Treated in Home Military Hospitals from August 1, 1915, to July 31, 1916." By Surg.-General Sir David Bruce. *The Lancet*, December 2, 1916.

"An Analysis of Cases of Tetanus Treated in Home Military Hospitals during August, September, and part of October, 1916." By Surg.-General Sir David Bruce. *The Lancet*, June 30, 1917.

"Fourth Analysis of Cases of Tetanus Treated in Home Military Hospitals during part of October, November, and part of December, 1916." By Surgeon-General Sir David Bruce. *The Lancet*. September 15, 1917.

"Note on the Incidence of Tetanus Among Wounded Soldiers." By Surg.-General Sir David Bruce. *British Medical Journal*, January 27, 1917.

"Importance of Early Prophylactic Injection in 'Trench Foot.'" By Surg.-General Sir David Bruce. *British Medical Journal*, January 13, 1917.

"Intramuscular *versus* the Intrathecal Route in the Treatment of Tetanus by the Injection of Antitoxin." By Surg.-General Sir David Bruce. *The Lancet*, May 5, 1917.

"A Report on Twenty-Five Cases of Tetanus." By Major H. R. Dean. *The Lancet*, May 5, 1917.

"Delayed Tetanus in Connexion with Fractures." By Capt. M. Foster, R.A.M.C. (T.). *British Medical Journal*, February 2, 1917.

"A Report on the Injection of Antitetanus Serum in Tetanus Cases." By F. W. Goadby, M.R.C.S., L.R.C.P., D.P.H., Cantab. *Journal, R.A.M.C.*, October, 1915.

"A Comparison of Subcutaneous with Intravenous and Intrathecal Administration of Tetanus Antitoxin in Experimental Tetanus." By Capt. F. Golla, R.A.M.C. (T.). *The Lancet*, May 5, 1917.

"The Prophylaxis of Tetanus." By Dr. A. T. MacConkey. *British Medical Journal*, December 11, 1915.

"Keeping Qualities of Therapeutic Serums." By Dr. A. T. MacConkey. *British Medical Journal*, January 6, 1917.

"A Note on the Reflexes in Tetanus." By Major A. G. Gibson, R.A.M.C. (T.). *The Lancet*, September 15, 1917.

J. C. Phelp & Son, Printers, Beulah Road, Walthamstow.